CONCLUSION ON PESTICIDE PEER REVIEW

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

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SUMMARY

Lenacil is one of the 84 substances of the third stage part B of the review programme covered by Commission Regulation (EC) No 1490/2002[3].

Lenacil was included in Annex I to Directive 91/414/EEC on 1 January 2009 pursuant to Article 11b of the Regulation (EC) No 1490/2002 (hereinafter referred to as 'the Regulation'). In accordance with Article 12a of the Regulation the European Food Safety Authority (EFSA) is required to deliver by 31 December 2010 its view on the draft review report submitted by the Commission of the European Communities (hereinafter referred to as 'the Commission') in accordance with Article 12(1) of the Regulation. This review report has been established as a result of the initial evaluation provided by the designated rapporteur Member State in the Draft Assessment Report (DAR). The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

Belgium being the designated rapporteur Member State submitted the DAR on lenacil in accordance with the provisions of Article 10(1) of the Regulation, which was received by the EFSA on 30 November 2007. The peer review was initiated on 08 January 2008 by dispatching the DAR for consultation of the Member States and the sole notifier Schirm GmbH. Subsequently, the comments received on the DAR were examined and responded by the rapporteur Member State in the reporting table. This table was evaluated by the EFSA to identify the remaining issues. The identified issues, as well as further information made available by the notifier upon request, were evaluated in a series of scientific meetings with Member State experts in April –May 2009.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in July 2009.

The conclusion was reached on the basis of the evaluation of the representative uses as herbicide as proposed by the notifier, which comprise foliar spraying in sugar beet and fodder beet for the control of grass and broad-leaved weeds. Full details of the GAP can be found in the list of end points in Appendix A.

The representative formulated product for the evaluation was 'Venzar 80 WP', a wettable powder (WP) containing 800 g/kg lenacil, registered under different trade names in Europe.

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1 On request from the European Commission, Question No EFSA-Q-2009-00242, issued on 25 September 2009.

2 Correspondence: praper@efsa.europa.eu

3 OJ L224, 21.08.2002, p.25, as amended by Regulation (EC) No 1095/2007 (OJ L246, 21.9.2007, p.19).

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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, however data gaps were identified for the determination of the accelerated storage stability and sprayability.

Adequate methods are available to monitor lenacil residues in food/feed of plant origin, soil and water however data gaps were identified for a confirmatory method for the determination of residues in water and for a residue method for air with a LOQ of at least 48 µg/m^3. It should also be noted that following the finalization of the residue definition for monitoring for soil, surface water and ground water, data gaps might have to be set for methods capable of analysing for the compounds in the residue definitions.

In mammals, lenacil is not acutely toxic via oral, dermal or inhalation routes; it is not a skin or eye irritant or skin sensitiser. In the short-term toxicity studies the rats and dogs were the most sensitive species showing alterations in the liver and thyroid function: the relevant oral No Observed Adverse Effect Levels (NOAELs) are 40.6 mg/kg bw/day and 44 mg/kg bw/day (rats and dogs, respectively;13-week studies). Lenacil is unlikely to be genotoxic. Increased incidence of malignant mammary adenocarcinoma were observed in rats and considered to be of relevance for humans. In mice, increased incidences of lung single alveolar tumours (adenoma and carcinoma) and multiple liver adenomas were observed and were considered of equivocal relevance for humans. Based on mammary gland and lung tumours, the classification Carc. cat.3, R40 'Limited evidence of a carcinogenic effect' was proposed. The relevant NOAEL from the long-term toxicity and carcinogenicity studies is 12 mg/kg bw/day (rat study). No specific effect on the reproductive parameters was found in multigeneration studies with rats: the relevant parental NOAEL is 81.9 mg/kg bw/day, the offspring NOAEL is 1727 mg/kg bw/day and the reproductive NOAEL is 4300 mg/kg bw/day. Tested in developmental toxicity studies, lenacil did not cause malformations in the rat and rabbits: the relevant maternal NOAEL in both species is 1000 mg/kg bw/day; the relevant developmental NOAELs are 1000 and 4000 mg/kg bw/day in rat and rabbits respectively (highest dose level tested). The Acceptable Daily Intake (ADI) of 0.12 mg/kg bw/day was derived from the chronic rat study applying a safety factor (SF) of 100. An Acute Reference Dose (ARfD) was considered not needed. The Acceptable Operator Exposure Level (AOEL) of 0.4 mg/kg bw/day (rounded) was based on the 13-week rat study supported by the 13-week dog study with a safety factor of 100. The operator exposure was estimated to be below the AOEL even without the use of personal protective equipment (German Model) and with gloves during mixing and loading and application (UK POEM Model). Worker and bystander exposure were estimated to be below the AOEL.

The metabolism of lenacil was investigated in sugar beet. Besides lenacil, the metabolite IN-KC943[4] formed by hydroxylation in the 7 position of lenacil and its glucosides and non-identified polar metabolites were found in sugar beet leaves. Since the most prevalent residue found in sugar beet metabolism was lenacil, the following residue definition was proposed for monitoring and risk assessment for root crops: lenacil only. A sufficient data base of residue trials from Northern and Southern Europe was submitted to propose an MRL for sugar beet (roots). Metabolism studies on rotational crops are not available. Based on the DT_{90} values found for the degradation of lenacil in soil in field studies, the PRAPeR experts meeting decided that metabolism studies on rotational crops are necessary to support the notified use.

Dietary burden calculations showed intake of lenacil residues through sugar or fodder beet roots and leaves slightly above the trigger value of 0.1 mg/kg feed. The PRAPeR experts meeting concluded that the intake was probably overestimated. Therefore, the majority of experts agreed that livestock metabolism studies should not be required.

[4] Metabolite IN-KC943: 3-cyclohexyl-7-hydroxy-6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,5*H*)-dione

A chronic dietary intake estimate was carried out by the rapporteur Member State. The TMDI was below 0.4% of the ADI for all considered consumer groups. An acute dietary intake estimate was not carried out as no ARfD was set.

In soil under aerobic conditions lenacil exhibits moderate to medium persistence forming the major soil metabolites IN-KF 313[5] (accounting for up to 14.7% of applied radioactivity (AR)), IN-KE 121[6] (accounting for up to 13.9% AR), unidentified metabolite 'Polar B' (accounting for up to 14.6% AR) and the unidentified 'Polars' (accounting for up to 12.5% AR). The proper characterisation of 'Polar B' and 'polars' or the assessments of the exposure of environment to these compounds were not available. Metabolite IN-KE 121 exhibits low to moderate persistence, while metabolite IN-KF 313 exhibits moderate to very high persistence. Mineralisation to carbon dioxide of the applied [4,7a-$^{14}C_2$]-lenacil accounted for 47.6-61.1% AR after 120 days (expressed as volatile compounds, which presumably consisted of mainly carbon dioxide). The formations of unextractable residues were a sink, accounting for 19.4-25.8% AR after 120 days. Lenacil exhibits medium to high mobility in soil. IN-KF 313 exhibits low to high, while IN-KE 121 exhibits very high mobility in soil. There was no indication that adsorption of either parent lenacil or the metabolites IN-KF 313 and IN-KE 121 was pH dependent. However the adsorption potential of IN-KF 313 was studied only in a narrow range of soil pH.

In natural sediment water systems lenacil exhibited high persistence (total system DT_{50} 122-103 days) degrading to the major metabolite IN-KF 313 (maximum 7.8% AR in the water phase and 10.7% in the sediment). The terminal metabolite, CO_2, was a minimal sink in the material balance accounting for only 3.8-4.8% AR at the study end. Residues not extracted from sediment accounted for 10.6-16.5% AR at study end. The necessary FOCUS surface water and sediment exposure assessments did not use exactly appropriate substance input parameters. However it was accepted that the available estimates could be used for the risk assessment discussed in this conclusion.

The potential for groundwater exposure from the applied for intended uses above the parametric drinking water limit of 0.1µg/L was concluded to be low in geoclimatic situations that are represented by the FOCUS groundwater scenarios by lenacil or IN-KE 121. No acceptable FOCUS simulations were available for the metabolite IN-KF 313. Based on the results of the available, non-agreed simulations, where the used degradation parameter was too favourable for this metabolite, in geoclimatic regions represented by Piacenza FOCUS groundwater scenario, contamination of groundwater above the 0.1 µg/L limit cannot be excluded. In a lysimeter study neither lenacil nor the known metabolites IN-KF 313 and IN-KE 121 were found in the leachates, but the annual average of the unidentified fractions, M1, M2 and M3 were present in the leachates above 0.1 µg/L.

The risk to non-target species (i.e. birds and mammals, bees, non-target arthropods, earthworms, soil macro- and micro-organisms, other non-target organisms, and biological methods for sewage treatment) was expected to be low, except for aquatic organisms. Algae and aquatic plants were the most sensitive organisms, and the effects were further assessed in higher tier studies. In particular, an outdoor microcosm field study on primary productivity and macrophytes was considered valid. This study showed several deficiencies, but it indicated a potential higher sensitivity of macrophytes and algae than the first-tier studies, therefore the experts considered it relevant for risk assessment. The experts agreed to consider the NOEC, expressed as measured concentration, as the most appropriate endpoint from this study, to be used with a safety factor of 2-5. However, a NOEC could not be finalised for either macrophytes or algae, and consequently it was not possible to finalise the risk assessment. A data gap was identified to address the sensitivity of *Charophyta* (the most sensitive species found in the microcosm study) and of algae. These further data should allow to define the endpoint from the outdoor microcosm study to be used for risk assessment.

[5] IN-KF 313: 3-cyclohexyl-6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4,5(3*H*)-trione
[6] IN-KE 121: 3-(4-oxocyclohexyl)-6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,5*H*)-dione

KEY WORDS

Lenacil, peer review, risk assessment, pesticide, herbicide

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BACKGROUND

Commission Regulation (EC) No 1490/2002[7] lays down the detailed rules for the implementation of the third stage of the work programme referred to in Article 8(2) of Council Directive 91/414/EEC. This regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the Draft Assessment Reports (DAR) provided by the designated rapporteur Member State (RMS).

Lenacil is one of the 84 substances of the third stage part B of the review programme covered by Commission Regulation (EC) No 1490/2002.

Lenacil was included in Annex I to Directive 91/414/EEC on 1 January 2009 pursuant to Article 11b of the Regulation (EC) No 1490/2002 (hereinafter referred to as 'the Regulation'). In accordance with Article 12a of the Regulation the European Food Safety Authority (EFSA) is required to deliver by 31 December 2010 its view on the draft review report submitted by the Commission of the European Communities (hereinafter referred to as 'the Commission') in accordance with Article 12(1) of the Regulation. This review report has been established as a result of the initial evaluation provided by the designated rapporteur Member State in the DAR. The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

In accordance with the provisions of Article 10(1) of the Regulation, the designated RMS, Belgium, submitted the DAR on lenacil (Belgium, 2007), which was received by the EFSA on 30 November 2007. Following an administrative evaluation, the DAR was distributed for consultation in accordance with Article 11(2) of the Regulation on 08 January 2008 to the Member States and to the sole notifier Schirm GmbH, as identified by the RMS.

The comments received on the DAR were evaluated and addressed by the RMS. Based on this evaluation, the EFSA identified and agreed on lacking information to be addressed by the notifier, as well as issues for further detailed discussion at expert level.

Taking into account the requested information received from the notifier, a scientific discussion took place in expert meetings in April–May 2009. 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 July 2009.

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

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 A.

The documentation developed during the peer review was compiled as a Peer Review Report (EFSA, 2009) 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 (revision 1-1; 02 March 2009),

[7] OJ L224, 21.08.2002, p.25, as amended by Regulation (EC) No 1095/2007 (OJ L246, 21.9.2007, p.19).

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 (revision 2-1; 25 September 2009).

Given the importance of the draft assessment report, including its Final Addendum (compiled version of July 2009 containing all individually submitted addenda) (Belgium, 2009) 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 Commission, the rapporteur Member State has made available amended parts of the draft assessment report 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 DAR together with the peer review report, both of which are publicly available.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Lenacil is the ISO common name for 3-cyclohexyl-1,5,6,7-tetrahydrocyclopentapyrimidine-2,4(3H)-dione (IUPAC).

Lenacil belongs to the class of substituted uracil herbicides. It is a photosynthesis inhibitor influencing the photosynthetic electron transport mechanisms. Lenacil is mainly absorbed via the root system but also by the leaves, it is translocated primarily via the xylem from the roots to the leaves. It is used to control a range of key annual weeds in sugar and fodder beet.

The representative formulated product for the evaluation was 'Venzar 80 WP', a wettable powder (WP) containing 800 g/kg lenacil, registered under different trade names in Europe.

The representative uses evaluated comprise foliar spraying to control grass and broad-leaved weeds in sugar beet and fodder beet, at growth stages of BBCH 10-31, in all EU countries, at maximum four applications, at maximum application rate per treatment of 0.5 kg a.s./ha, with interval between applications of 1-2 weeks.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of technical lenacil is 975 g/kg. There is no FAO specification for lenacil.

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 lenacil or the representative formulation, however the following data gaps were identified:

- the material quantified under "loss on drying" should be quantified by specific methods

- accelerated storage stability test of the preparation

- a sprayability test

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

Adequate analytical methods are available for the determination of lenacil in the technical material and in the representative formulation (RP and NP HPLC-UV) as well as for the determination of the impurities in the technical material (HPLC-DAD, ICP-OES).

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

Residues of lenacil in food of plant origin can be monitored by HPLC-MS/MS with a LOQ of 0.02 mg/kg (sugar beet leaf and root). Sufficient data were presented to demonstrate the applicability of a multi-method in the light that another fully validated method is available.

An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed (see 3.4).

Residues of lenacil in soil can be monitored by GC-MS with a LOQ of 0.05 mg/kg or residues of lenacil and metabolite IN-KF-313 by HPLC-MS/MS with LOQs of 0.02 mg/kg for each compound. It should however be noted, that following the finalization of the residue definition for monitoring, a data gap might have to be set for a method capable to analyse for the compounds in the residue definition.

HPLC-DAD method is available to monitor residues of lenacil in surface water and drinking water with LOQs of 0.1 µg/l, however, the experts at the PRAPeR 66 meeting (April 2009) identified a data gap for a confirmatory method for the determination of residues in water. It should also be noted that following the finalization of the residue definition for monitoring for surface water and ground water, data gaps might have to be set for methods capable of analysing for the compounds in the residue definitions.

The meeting also concluded that a new air method was required with a LOQ of at least 48 µg/m^3.

Analytical methods for the determination of residues in body fluids and tissues are not required as lenacil is not classified as toxic or highly toxic.

2. Mammalian toxicity

The mammalian toxicology of lenacil was discussed during the PRAPeR expert's meeting (PRAPeR 69, round 14) in May 2009 on the basis of the DAR and the Addendum to Vol.3 B.6 (February 2009) from the Final Addendum to the DAR. After the expert's meeting, an Addendum 2 to Vol.3 B.6 (May 2009) was submitted, and is compiled in the Final Addendum.

It was agreed during the commenting and reporting table phase that batches used in the toxicological studies cover the current technical specification.

2.1. Absorption, distribution, excretion and metabolism (toxicokinetics)

Lenacil oral absorption was discussed during the meeting. It was agreed to be higher than 80% based on excretion in urine and faeces minus parent compound after application of repeated low dose. It is uniformly distributed and shows a low potential for bioaccumulation. The excretion is almost complete in 48 h and takes place via urine and faeces. The main pathway of metabolism is hydroxylation.

2.2. Acute toxicity

Lenacil is not acutely toxic to the rats via oral, dermal (LD50 higher that 5000 and 2000 mg/kg bw, respectively) or inhalation (LC50>5.12 mg/l of air-nose only/4h) routes. It is not a skin or eye irritant or skin sensitiser in the Guinea Pig Maximization Test.

2.3. Short-term toxicity

Oral short-term toxicity has been studied in dietary 13-week studies in rats, dogs and mice, with the rat and dog being the most sensitive species. The target organs were the white blood cells (rat, mice) and the thyroid and liver (rat, dog). During the meeting the relevant NOAEL from the 90-day mice study was discussed and agreed to be 157 mg/kg bw/day, based on increase liver weight in females treated at dose level of 787 mg/kg bw/day. The relevant NOAELs are 40.6 mg/kg bw/day and 44 mg/kg bw/day in rats and dogs respectively.

No dermal and inhalation studies were submitted or required.

2.4. Genotoxicity

Based on a set of adequately conducted *in vitro* and *in vivo* assays it can be concluded that lenacil is unlikely to be genotoxic.

2.5. Long-term toxicity and carcinogenicity

Long-term toxicity and carcinogenicity of lenacil has been studied in rats (104-weeks) and mice (18-month).

In **rats**, the systemic NOAEL is 118 mg/kg bw/day based on liver and thyroid effects at 1223 mg/kg bw/day (increased weight and hypertrophy/vacuolation in the liver and relative weight increase in the thyroid and increase TSH). In **mice**, the systemic NOAEL is 332 mg/kg bw/day based on increased liver weight associated with centrilobular hypertrophy at 977 mg/kg bw/day.

During the meeting the carcinogenic properties of lenacil were discussed. Thyroid and mammary gland tumours were observed in female rats. Thyroid follicular cell adenomas were within laboratory historical control data and C-cell tumours were considered as age and gender-dependent. Therefore, thyroid tumours were not considered relevant for human exposure. Nevertheless, the incidence of malignant mammary adenocarcinoma was above the historical control data of the laboratory and the experts agreed to consider them as relevant for humans. The carcinogenic NOAEL in rats was established at 12 mg/kg bw/day.

With regard to mice, liver and lung tumours were observed in males treated at the high dose level. The incidence of multiple liver adenomas was outside the laboratory historical control range. The incidence of lung single alveolar adenoma was above the laboratory historical control data, but the incidence of lung single alveolar carcinoma was within the laboratory historical control data. When taken together, the combined lung adenoma and carcinoma incidence was outside the laboratory historical control data but it is presumably because of adenoma incidence. Lung and liver tumours were considered of equivocal relevance for humans. The carcinogenic NOAEL in mice was established at 332 mg/kg bw/day.

In the Addendum (February 2009), the RMS proposed the classification and labelling of lenacil as Carc. Cat 3, R40. The experts agreed.

2.6. Reproductive and developmental toxicity

In a two-generation reproduction study in rats, the parental NOAEL was established at 81.9 mg/kg bw/day based on effects in the thyroid and the liver. In the DAR, the offspring NOAEL was 1727 mg/kg bw/day based on decreased body weight gain during lactation at 4300 mg/kg bw/day. In addition, according to the RMS, since this effect was observed before the offspring could consume solid food it suggested a reproductive effect via lactation, and the RMS proposed the classification as R64 and a reproductive NOAEL of 1727 mg/kg bw/day. The meeting concluded that considering the very high dose level applied in the study (4300 mg/kg bw/d which exceeds the 1000 mg/kg bw/d limit dose for reproductive toxicity studies) the decrease in offspring weight gain during lactation was deemed insufficient to justify R64 and did not consider the effects as reproductive but offspring toxic effects. Therefore, the offspring and reproductive NOAELs were considered to be 1727 and 4300 mg/kg bw/day, respectively.

Tested in developmental toxicity studies, lenacil did not cause malformations in the rat and rabbit up to dose levels of 1000 and 4000 mg/kg bw/day, respectively, even in the presence of maternal toxic effects in rabbit (reduced body weight gain) at 4000 mg/kg bw/day. As a result, the NOAEL for maternal toxicity is 1000 mg/kg bw/day in both species and the NOAEL for developmental toxicity is 1000 and 4000 mg/kg bw/day in rat and rabbit respectively (highest dose level tested).

2.7. Neurotoxicity

No signs of neurotoxicity. No data on delayed neurotoxicity are available or required since lenacil does not belong to the family of organophosphates.

2.8. Further studies

During the meeting, the toxicological relevance of the plant metabolite, IN-KC943[8], was discussed. The experts agreed that the metabolite is structurally closely related to the major metabolite of lenacil in the rat identified as a hydroxylated metabolite of lenacil with the OH group on C3 or C4 (found in urine and faeces in rat) and therefore is covered by the toxicological studies of the parent compound. If the metabolite were included in the residues definition the same trigger values of the parent compound could be applied.

Mechanism studies were performed to clarify the effects of lenacil on thyroid in rats. A NOAEL of 41 mg/kg bw/day was selected based on the slight increased incidence of staining of liposfucin in the follicular epithelium of thyroids of female rats treated by dietary administration at 412 mg/kg bw/day during 13 weeks. In addition, the perchlorate-disharge test in female rats treated during 20 weeks showed no effect on the uptake and organification of iodine. Nevertheless, not enough information was provided for interpreting changes in thyroid hormone levels in terms of mechanism of toxicant action. Therefore, the effects were considered relevant for humans and were taken into account for settings of NOAELs.

EFSA note: Pending the outcome of the ground water exposure assessment there might be a need to address the toxicological relevance of metabolites (see 4.1 and 4.2.2).

2.9. Medical data

There were no reports of adverse effects and/or poisoning under work place conditions or under experimental agricultural use.

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

ADI

In the DAR, the RMS proposed to set an ADI of 0.14 (0.12-0.16) mg/kg bw/day based on the long-term study in the rat and a safety factor of 100. The meeting agreed to the proposal but considered that the value should be the lower value of the range, 0.12 mg/kg bw/day.

AOEL

In the DAR, the RMS proposed to set an AOEL based on the 90-day mice study. Since the NOAEL from this study was reconsidered during the meeting (see point 2.3) the AOEL agreed by the experts was 0.4 mg/kg bw/d based on 90-day rat study supported by the 90-day dog study and a safety factor of 100.

ARfD

According to the toxicological profile of lenacil, the setting of an ARfD was not considered necessary. The experts agreed.

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[8] IN-KC943: 3-cyclohexyl-7-hydroxy-6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,5*H*)-dione

2.11. Dermal absorption

During the commenting and reporting table phase, dermal absorption values of 1 and 15.5% for the concentrate and diluted formulation 'Venzar 80 WP', respectively, were agreed, based on a dermal *in vitro* human skin study.

2.12. Exposure to operators, workers and bystanders

'Venzar 80 WP' is a wettable powder formulation containing 800g/kg lenacil. It is intended for application through hydraulic field crop sprayers to sugar beet. The recommended application rate is a maximum of 500 g a.s/hectare.

New operator, worker and bystander exposure estimates were submitted by the RMS in the Addendum 2 (May 2009) according to the input parameters and AOEL agreed during the PRAPeR meeting. Results are summarised below.

Operator exposure

Estimated systemic exposure (mg/kg bw/day) was performed according to calculations with the German and UK POEM models. The default body weight of operator is 70 kg in the German model and 60 kg in the UK-POEM model. The treated area is 50 ha/day (UK model) or 20 ha/day (German model) for tractor-mounted sprayer.

The estimated operator exposure is below the AOEL even in the absence of PPE in the German model. In the UK POEM the estimated operator exposure is below the AOEL with the use of gloves during mixing/loading and application.

Estimated exposure presented as mg/kg bw/day and as % of AOEL (0.4 mg/kg bw/day), according to calculations with the German and UK-POEM models:

		Total Systemic Exposure mg/kg bw/d % of AOEL	
		German Model	**UK POEM**
Sugar beet (Tractor mounted boom sprayer)			
	No PPE	0.06388 16%	0.415 >100%
	PPE *	0.0470 12%	0.132 33%

* PPE: gloves M/L + A

Worker exposure

Worker exposure to lenacil during re-entering the application area for field inspection operations has been estimated using the coefficients from the German BBA[9] resulting in 0.019375 mg/kg bw/day which is 4.8% AOEL.

Bystander exposure

[9] Krebs B. *et al.*, (1998) Uniform Principles for Safeguarding the Health of Worker Re-entering Crop Growing Areas after Application of Plant Protection Products. (Bulletin of the German Plant Protection Service) Nachrichtenblatt des Deutschen Pflanzenschutzdienstes.10/98;Vol 50, Verlag Eugen Ulmer , Stuttgart, Germany

For the estimation of bystander exposure, the RMS used assumptions from Lloyd and Bell, 1983[10], resulting in 0.00089 mg/kg bw/day which is 0.23% AOEL.

3. Residues

The active substance lenacil was discussed at the PRAPeR experts meeting for residues (PRAPeR 70, round 14) in May 2009.

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

To support notified uses on sugar and fodder beet, a metabolism study on sugar beet was submitted. Lenacil radio-labelled in the pyrimidine ring was applied twice with a total application rate of approximately 500 g a.s./ha which is in line with the notified cGAP. The growth stages at the time of applications of BBCH 14 and 16 were earlier than the critical notified growth stage of BBCH 31. The RMS considered the study as acceptable, as a change of the metabolic pattern is not expected for an application at a later stage. This would result in higher levels of TRR, but a less extensive metabolism.

The TRR in root samples was maximum 0.03 mg/kg and therefore too low for identification of metabolites. Moderate metabolism was observed in samples of foliage. Lenacil, which was the main component of the TRR in all samples, declined from 96% of TRR (7 mg/kg) at the day of the first application to 28 % of TRR (0.04 mg/kg) 115 days after the second application. The only identified metabolites were IN-KC943 formed by hydroxylation in position 7 of lenacil (max. 3% of TRR) and its glucosides (max. 10.7% of TRR). The polar fraction of metabolites, some of which could be hydrolysed by β-glucosidase, accounted for max. 38% of TRR (0.06 mg/kg). As no single polar metabolite exceeded 10% of TRR, no attempts were made to further characterise or identify them.

The PRAPeR experts meeting 69 on Mammalian Toxicology concluded that IN-KC943 is structurally closely related to the major metabolite of lenacil in the rat identified as a hydroxylated metabolite of lenacil with the OH group on C3 or C4 (found in urine and faeces in rat) and therefore is covered by the toxicological studies of the parent compound. If the metabolite were included in the residue definition the reference values of lenacil could be applied.

The PRAPeR meeting 70 discussed if the metabolite IN-KC943 and its metabolites should be included in the residue definition. For the notified use, parent lenacil was the most prevalent residue in leaves. The metabolic pathway in roots is not expected to be different from metabolism in leaves. Therefore, the following residue definition for monitoring and risk assessment for root crops was proposed: lenacil only. However, it was concluded that the residue definition should be re-discussed for future uses including further uses on other root crops or spinach.

A total of seven residue trials carried out in Northern Europe in the years 1995 and 2001 were submitted on sugar beet. Four of the trials were regarded as acceptable. The application was carried out at BBCH 37, which is later than the notified cGAP (BBCH 31). However, residues below the LOQ (0.02 mg/kg) were found in all root samples. The trials are supported by storage stability studies and the analytical method used is fully validated. Residue levels found in foliage ranged from < LOQ (0.02 mg/kg) to 0.04 mg/kg. Three of the trials were performed at GS 14-19, which is within the notified GAP, but earlier than then the cGAP (BBCH 31). They were regarded as not acceptable, as

[10] Lloyd, G.A. and Bell, G.J. (1983) .Hydraulic nozzles: comparative spray drift study. UK Ministry of Agriculture, Fisheries and Food. (Report of a study carried out in 1983 in association with the British Agrochemicals Association).

the samples were analysed after 26 months after the harvest and therefore are not supported by storage stability data (see below).

Three trials in sugar beet were carried out in the years 2002 and 2005 in Southern Europe with application at BBCH 31 and BBCH 38, respectively. They were regarded as acceptable. Residues below LOQ (0.02 mg/kg) were found in all root samples. The trials are supported by storage stability data and the analytical method used was fully validated. Residue levels in sugar beet foliage were below LOQ (0.02 mg/kg) after application at BBCH 31 and 0.03 mg/kg in the trial with application at BBCH 38.

As residues below the LOQ were found in all samples of sugar beet roots, the submitted residue trials were regarded as sufficient to support the notified use in Northern and Southern Europe.

Submitted data on freezer storage stability showed that lenacil is stable in sugar beet leaves and roots for 254 days.

Since no significant residues were found in sugar beet roots, data on the effects of processing on the nature of the residues or on residue levels are not required.

3.1.2. Succeeding and rotational crops

Confined rotational crop studies are not available. According to the RMS the notifier recommended succeeding crops should not be planted or drilled until at least 120 days after application of lenacil because of its phytotoxicity. If crop failure occurred during this period only sugar beet, red beet or spinach could be planted. However, no data on phytotoxicity tests have been submitted by the notifier.

DT_{90} values of 61 to 291 days were found for the degradation of lenacil in soil in field studies carried out in Germany, France and Spain. The study with a DT_{90} of 291 days was carried out under rather extreme climatic conditions in Spain. However, these conditions were regarded as a possible scenario by the PRAPeR experts' meeting 67 on fate and behaviour. Therefore, the PRAPeR 70 meeting concluded that a metabolism study on rotational crops taking into account possible phytotoxicity problems is necessary.

3.2. Nature and magnitude of residues in livestock

Dietary burden calculations have been carried out taking into account the highest residue level found in sugar beet leaves of 0.04 mg/kg and the LOQ in sugar beet roots of 0.02 mg/kg. The intake for chicken, dairy cattle, beef cattle and pigs were calculated to be 0.020, 0.105, 0.135 and 0.123 mg/kg feed (DM).

Metabolism studies in livestock were not submitted by the notifier. Metabolism studies on animals are required when pesticide use may lead to residues ≥ 0.1 mg/kg in livestock feed. The PRAPeR expert meeting discussed the necessity of such studies. Whereas metabolism studies for ruminants are required on the basis of the intake calculation carried out, the experts concluded that the intake was probably overestimated. The residue level of 0.04 mg/kg was found after application of lenacil at growth stage BBCH 37/38, which is later that the notified critical growth stage. Residues in roots are likely to be much lower than the LOQ of 0.02 mg/kg. Therefore, the majority of experts agreed that livestock metabolism studies should not be required.

3.3. Consumer risk assessment

The RMS provided a chronic consumer risk assessment for chronic exposure in the revised list of end points (not peer-reviewed) taking into account the ADI of 0.12 mg/kg bw/day and intake of sugar beet (root) with lenacil residues at the LOQ of 0.02 mg/kg. For the WHO European diet a TMDI of 0.02% of ADI was calculated. A calculation carried out with the EFSA PRAPeR model (PRIMO, rev. 2) showed the diet for UK toddlers (TMDI = 0.4% ADI) as the most critical model for the chronic intake.

EFSA notes that the chronic risk assessment might need to be updated, if further investigations show that residues of lenacil are expected in rotational crops (see section 3.1.2).

An acute risk assessment was not required, as no ARfD was set.

3.4. Proposed MRLs

In accordance with the proposed residue definition for monitoring (lenacil) the following MRL was proposed:

Sugar beet (root) 0.02* mg/kg

* MRL is proposed at the limit of quantification (LOQ).

If further investigations show that residues of lenacil are expected in rotational crops (see section 3.1.2), it might be necessary to propose MRLs for rotational crops.

The PRAPeR 70 meeting concluded that metabolism studies on livestock should not be required to support the notified use on sugar beet and fodder beet (see section 3.2). Therefore, neither a residue definition for monitoring nor MRLs for animal matrices were proposed.

4. Environmental fate and behaviour

Lenacil was discussed by the Member State experts for environmental fate and behaviour in the PRAPeR experts' meeting 67 in April 2009 on the basis of the revised Volume 3 Section B8 of the Draft Assessment Report (March 2009). The original DAR was prepared in 2007 (November 2007), but this document was updated (leading to the revised DAR) after the comments received on the DAR were examined and responded by the rapporteur Member State.

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

Appropriate studies summarized either in the route of degradation or in the rate of degradation chapter of the revised DAR were available to study the degradation pathway of lenacil in aerobic soils. The five acceptable soil experiments (OC 1.0-3.3%, pH 5.4-6.4, clay 8.2-21.3%) were carried out under aerobic conditions in the laboratory (20°C, 40% maximum water holding capacity (MWHC)) in the dark. The formation of residues not extracted were a sink for the applied [4,7a-$^{14}C_2$]-lenacil (19.4-25.8% of the applied radioactivity (AR) after 120 days). Volatile compounds including presumably mainly carbon dioxide, accounted for 47.6-61.1% AR after 120 days. The major (>10% AR) extractable breakdown products presented were IN-KE 121[11] (maximum occurrence 9.2-13.9% AR at 14-30 days), IN-KF 313[12] (maximum occurrence 8.5-14.7% AR at 7-14 days) and the unidentified metabolite 'Polar B' (maximum occurrence 6.8-14.6% AR at 60-91 days). Furthermore in one soil

[11] IN-KE 121: 3-(4-oxocyclohexyl)-6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,5*H*)-dione
[12] IN-KF 313: 3-cyclohexyl-6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4,5(3*H*)-trione

there was also a minor non-transient unidentified breakdown product denoted 'M15.0'[13] that accounted for more than 5%AR at two consecutive sampling times. Based on the attempts made by the notifier to identify this metabolite, this product was characterised as an oxo-isomer of lenacil, which is formed by the oxidation of the cyclohexyl ring. The identified metabolite IN-KE 121 is also an oxo-isomer of lenacil (7-oxo-lenacil), but from the available information the conformity of these transformation products could not be fully confirmed. The available information on the identity and the further use of the degradation data of the metabolite M15.0 was discussed at the PRAPeR 67 meeting. The experts agreed that M15.0 is either identical to IN-KE 121 or is a positional isomer of IN-KE 121 with the keto-function on the cyclohexane ring, and agreed moreover that the exposure assessment for IN-KE 121 would probably cover the assessment for M15.0 even with respect to degradation. Therefore no separate exposure assessment for groundwater was required for the metabolite M15.0, which is probably the metabolite IN-KE 121, and was not included in the residue definition for the exposure assessment for groundwater.

One experiment was repeated at 10 ºC in which metabolite IN-KE 121 reached 7.8% AR (on day 30), metabolite IN-KF 313 reached 9.4% AR (on day 60) and the amount of the breakdown product denoted 'Polars' was observed above 10% AR (maximum occurrence 12.5% AR at 120 days). Unextractable residue amounted up to 20.9% AR and volatiles (presumably consisting of mainly carbon dioxide) reached a maximum of 24.4% AR after 120 d; at the end of this experiment.

A data gap was agreed by the meeting of experts at PRAPeR 67 regarding the need for further characterisation of 'Polar B' and 'polars'. Depending on the outcome of any information submitted to address the data gap, exposure assessments for these unidentified metabolites may be necessary.

No anaerobic soil degradation study was available; however extended anaerobic soil conditions would not be expected for the intended use applied for (post-emergence application on sugar and fodder beet). In a laboratory soil photolysis study no major photodegradation products were identified.

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

The rate of degradation of lenacil was estimated from the results of the studies described in 4.1.1. In the original DAR the derivation of the degradation endpoints were commented since discrepancies were identified in the classifications of some soils and in the normalization procedure; moreover the invalidity of one study using US soils was also questioned. In the revised DAR, these discrepancies were corrected and the meeting of experts agreed that the new information regarding the degradation endpoints presented in the revised DAR, were acceptable. The meeting of experts confirmed that the rate study of the parent, which used three US soils is invalid and the results from these experiments were not used further. Single first order (SFO) DT_{50} values at 20°C and 40% maximum water holding capacity (MWHC) were calculated to be 11-25 days (number of soils considered was 5). After normalization of these values to FOCUS reference conditions (20°C and pF2 soil moisture content), the range became 11-18 days (geometric mean that is appropriate for use in FOCUS modelling is 14.4 days).

The rate of degradation of the major soil degradation product, IN-KF 313 was estimated from the results of the studies with the parent compound, described in point 4.1.1 and in 3 additional US soils (OC 0.52-1.39%, pH 6.3-6.8, clay 7.6-22.0%) at 25°C and pF 2.5 soil moisture, where IN-KF 313 was applied as test substance. The meeting of experts discussed and agreed that the rate study with the US soils is valid and the results should be used further despite the significantly higher persistency observed in these experiments. Single first order DT_{50} values were calculated to be between 3-350 days (20°C or 25°C and 40% MWHC or pF2.5 soil moisture content, n=8). After normalisation to

[13] M15.0: 3-(?-oxocyclohexyl)-6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,5*H*)-dione

FOCUS reference conditions (20°C and pF2 soil moisture content) this range of single first order DT_{50} became 3-444 days (geometric mean that is appropriate for use in FOCUS modelling is 41 days).

Degradation parameters for the metabolite IN-KE 121 were also estimated from the results of the studies with the parent compound (described in point 4.1.1). It was agreed by the meeting of experts at PRAPeR 67 that the degradation parameters calculated for the metabolite M15.0 from one soil experiment should be included in the dataset of the metabolite IN-KE 121 (for the discussion regarding this issue see point 4.1.1). Single first order (SFO) DT_{50} values at 20°C were calculated to be 4-12 days (number of soils considered were 5). After normalization of these values to FOCUS reference conditions (20°C and pF2 soil moisture content), the range became 4-11 days (geometric mean that is appropriate for use in FOCUS modelling is 6.4 days).

Based on the available data sets including some information from the physical-chemical section of the revised DAR, the experts at the meeting (PRAPeR 67) considered that the degradation of lenacil and its identified metabolites is not dependent on the soil pH, however it was noted by the meeting that the pH range of the soils investigated for aerobic degradation was limited.

Field soil dissipation studies were provided from 4 sites in Europe (2 in Germany, 1 each in France and Spain) where spray applications (one for each site) were made in June or July. Using the residue levels of parent lenacil determined over the top 10 cm (no residues were detected below 10 cm soil layer), single first order DT_{50} were between 18-88 days. Small residues (< LOQ) of the major soil metabolite IN-KF 313 were detected only in a few cases in the top 10 cm layer, therefore no decline kinetics were calculated for this metabolite. The RMS considered the results from the Spanish trial, which gave the longest DT_{50} of 88 days for lenacil, as an outlier regarding the hot and dry weather conditions during the first three months of this experiment. The meeting of experts at PRAPeR 67 agreed that the conditions of the Spanish trial can occur in reality and therefore there is no reason to discard this experimental site and the results should be retained. This longest available field SFO soil DT_{50} of 88 days was agreed by the experts from the Member States for use in PECsoil calculations for lenacil, when time weighted averages (TWAs) are needed. The experts also agreed that for the metabolites the qualitative PECsoil calculations based on the initial PEC of the parent is appropriate in this case, but the maximum observed percentage from the laboratory experiments should be used instead of the kinetic formation fraction.

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

The adsorption/desorption of lenacil was investigated in 7 soils at 20°C or 25°C in satisfactory batch adsorption experiments. K_{Foc} values varied from 75 to 254 mL/g, (median 83 mL/g) indicating that lenacil exhibits high to medium mobility in soil. Freundlich coefficients ranged from 0.86 – 0.94 (median 0.89, the value associated with the median K_{Foc} of 0.88 was used for FOCUS PECgw simulations).

The adsorption/desorption of the metabolites IN-KE 121 and IN-KF 313 was investigated in three soils. Calculated adsorption K_{Foc} for IN-KE 121 varied from 30.5-43.5 mL/g (mean 38 mL/g) and the 1/n values ranged from 0.92 – 0.96 (mean 0.95). There was no indication of any relationship between adsorption and any soil characteristic including pH.

Calculated adsorption K_{Foc} for IN-KF 313 varied from 79 - 824 mL/g (mean 557 mL/g) and the 1/n values ranged from 0.67 – 1.0 (mean 0.89). The meeting of experts concluded that two soils out of the three were very similar (in terms of organic carbon content, pH and texture), moreover the pH range of the three soils was too narrow (pH 6.3-6.8) and not representative of the agronomic conditions for sugar beet. pH dependency cannot be established nor excluded based on the available data with this narrow pH range. Therefore a data gap was identified by the meeting of experts at PRAPeR 67 for a soil batch adsorption study in one soil for IN-KF 313 under environmentally relevant alkaline conditions.

In a BBA guideline, a four-year lysimeter study (1.1 m depth soils monoliths of loamy sand soil) was carried out in Germany where a split application (200 g/ha + 300 g/ha) was made in June. Sugar beet was grown in the lysimeters in the first year and the subsequent crop rotation was winter wheat and winter barley. Only unidentified fractions were present in the leachates that were shown by chromatography to have different chromatographic behaviour from lenacil or the known metabolites IN-KF 313 and IN-KE 121. Three of these unidentified fractions, M1, M2 and M3 were present in the leachates above 0.1 µg/L in the first year (0.200-0.519 µg/L) and M1 and M3 in the second year as well. An assessment in a position paper submitted by the notifier, which is included in the revised DAR, indicated that these metabolites might be ring opening products/molecule fragments and might be of no concern. However these metabolites revealed a high potential for leaching and were not identified. Therefore the meeting of experts at PRAPeR 67 set a data gap for further characterisation of M1, M2 and M3 found in the leachates of the lysimeters.

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

Lenacil was essentially stable under sterile hydrolysis conditions at 50°C at pH 4, 7 and 9. The hydrolytical DT_{50} at 25°C was estimated to be greater than one year.

The aqueous photolysis of lenacil was investigated in a laboratory study under sterile pH 5 conditions, where negligible degradation was observed (DT_{90} > 1 year). The quantum yield for lenacil calculated from this study was 2.62×10^{-7}.

A ready biodegradability test (OECD 301B) indicated that lenacil is 'not readily biodegradable' using the criteria defined by the test.

Information on degradation of lenacil in water sediment systems was available from a water-sediment study, where two systems were used at 20°C in the laboratory (water pH 8.3 and ~8.0, sediment pH ~7.5 and ~7.0). Lenacil exhibited high persistence, degrading in the total systems with estimated single first order DT_{50} of 122 and 103 days (DT_{90} 405-342 days).

IN-KF 313 was the only major metabolite, which peaked in the sediment phase on day 120 reaching the maximum levels of 10.7% AR in the sediment phase of one of the systems (only max. 3% AR was observed in the sediment of the other system at day 88). In the water phase, this metabolite reached the maximum of 7.5-7.8 % AR during the study. The terminal metabolite, CO_2, was a minimal sink in the material balance, accounting for only 3.8-4.8% AR in these systems by the study end. Residues not extracted from sediment accounted for 10.6-16.5% AR at study end.

FOCUS surface water modelling was evaluated at step 3 for lenacil and for the metabolites IN-KE 121 and IN-KF 313 in the original DAR (November 2007). Some input parameters were changed during the peer review, but new calculations were not provided either before or after the meeting of experts. The RMS proposed in the revised DAR (March 2009) and in the evaluation table rev 2-0 to only repeat these calculations for national product authorisations. Moreover the risk assessment for aquatic organisms could not be finalised (for details see point 5.2 Risk to aquatic organisms). However an open point was set for the RMS for new PECsw/sed calculations for the metabolite IN-KF 313 by the meeting of experts PRAPeR 67. After the meeting, EFSA performed these calculations at FOCUS step 2 level, using the input parameters agreed by the meeting of experts at PRAPeR 67. These calculations are included in Appendix A of this conclusion.

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

FOCUS surface water modelling for lenacil and for the metabolites IN-KE 121 and IN-KF 313 using FOCUS PRZM 2.4.1 and FOCUS PEARL 2.2.2 were included in the original DAR (November 2007). Since some input parameters were questioned during the peer review, a new set of calculations were included in the revised DAR (March 2009). In these simulations the applied for representative use of spring applications to sugar beet was simulated only with FOCUS PEARL 3.3.3 model using the following input parameters: lenacil single first order DT_{50} 14.4 days, K_{Foc} 83 mL/g, 1/n=0.88; IN-KE 121 single first order DT_{50} 7.4 days, formation fraction from lenacil 0.43, K_{Foc} 38 mL/g, 1/n=0.95. The meeting of experts at PRAPeR 67 agreed with these simulations, however it is noted that for the metabolite IN-KE 121 the finally agreed soil DT_{50} was 6.5 days and the agreed formation fraction from lenacil was 0.48. The simulations provided for the metabolite IN-KF 313 in the revised DAR (March 2009) used significantly lower soil DT_{50} (11.2 days instead of 41 days, which is the agreed value), therefore an open point for the RMS was agreed by the meeting of experts at PRAPeR 67 for a new PECgw modelling for the metabolite IN-KF 313. Since no new simulations were performed, a data gap was set by EFSA for new PECgw modelling for the metabolite IN-KF 313 using the agreed input parameters by the expert's meeting PRAPeR 67.

In the simulations parent lenacil and metabolite IN-KE 121 was calculated to be present in leachate leaving the top 1 m soil layer at 80th percentile annual average concentrations of <0.01 µg/L or <0.1 µg/L, respectively. Based on the results of the available, non agreed simulations for the metabolite IN-KF 313, in geoclimatic regions represented by Piacenza FOCUS groundwater scenario, contamination of groundwater above the 0.1 µg/L limit cannot be excluded.

4.3. Fate and behaviour in air

The vapour pressure of lenacil (1.7 x 10-9 Pa at 25°C) means that lenacil would be classified under the national scheme of The Netherlands as very slightly volatile; indicating losses due to volatilisation might be expected to be minimal. Calculations using the method of Atkinson (using the software APOWIN v.1.88) for indirect photo oxidation in the atmosphere through reaction with hydroxyl radicals resulted in an atmospheric half-life estimated at 2.8 hours (assuming an atmospheric hydroxyl radical concentration of 1.5x106 radicals cm-3). This half-life indicates that the proportion of lenacil which is volatilised is unlikely to be subject to long-range atmospheric transport.

5. Ecotoxicology

Lenacil was discussed at the PRAPeR experts' meeting 68 on ecotoxicology in May 2009 on the basis of the Draft Assessment Report (DAR) updated in April 2009 and the Addendum to Vol.3 B.9 (April 2009) from the Final Addendum to the DAR.

The representative use evaluated was as a herbicide in sugar beet and fodder beet; the maximum application rate was 0.5 kg a.s./ha per season, 4 applications. The representative formulation was "Venzar 80 WP".

5.1. Risk to terrestrial vertebrates

Acute, short-term and long-term toxicity studies on birds were available for technical lenacil indicating a low toxicity (LD50 and LC50 greater than the highest tested dose and NOEC equal to the highest tested dose).

On the basis of first-tier risk assessment, all the TER values were above the Annex VI triggers, indicating a low risk to birds.

On the basis of mammalian toxicity data (i.e. acute oral toxicity and 2-generation study on rat), the first-tier risk assessment also indicated a low risk for other terrestrial vertebrates.

5.2. Risk to aquatic organisms

Several studies (both acute and long-term) were available on aquatic organisms (fish, daphnia, sediment dwelling organisms, algae and higher plants) for technical lenacil, formulation product and the metabolites IN-KE 121 and IN-KF 313.

Algae and aquatic plants were the most sensitive organisms. The endpoint driving the risk assessment was observed in a study with lenacil and *Pseudokirchneriella subcapitata* (72-h E_bC_{50} = 7.7 µg/L). A study with the formulated product and *Pseudokirchneriella subcapitata* was available but was considered to be not valid by the experts, since the analytical measurements were not performed (72-h E_bC_{50} = 6.72 µg/L). A data gap was identified to provide a new study with the formulation product and *Pseudokirchneriella subcapitata* (see further comments to this data gap below). The studies with the metabolites IN-KE 121 and IN-KF 313 and *Pseudokirchneriella subcapitata* showed a lower toxicity than the parent.

An indoor microcosm study with macrophytes and an outdoor field study on primary productivity and macrophytes were performed. The former was considered not valid by the experts. The outdoor field study showed a higher sensitivity than the standard first-tier studies and therefore it was considered relevant for risk assessment, even though it showed several deficiencies, as widely discussed during the experts' meeting. A new higher tier study was considered not necessary.

Outdoor field study on primary productivity and macrophytes/**Macrophytes**:

Elodea canadensis showed recovery within 8 weeks at treatment level of 22.1 µg a.s./L, therefore, the RMS proposed a NOAEC of 22.1 µg a.s./L (nominal concentration) as relevant for risk assessment.

The experts noted that the maximum measured concentration (10.17 µg a.s./L after 3 days) was lower than the proposed NOAEC of 22.1 µg a.s./L. No explanations for the delayed maximum concentration were available. Therefore, the experts agreed that the endpoint should be expressed as measured concentration.

The experts questioned the potential for recovery because a) competition is not usually addressed in studies with potted plant, b) the study was performed quite late in the season (application in July) and the control showed a decline in some species and c) the study was performed with a single application and did not cover the supported use (4 applications per season). Therefore, the experts considered that it was more appropriate to use the NOEC instead of the NOAEC.

The experts noted that for one species (*Charophyta*), the NOEC was not determined (NOEC<0.4 µg a.s./L). The RMS argued that this species was not introduced in the test system but arrived spontaneously. For all the potted species present in the test, the NOEC was determined (NOEC of 5.81 µg a.s./L for *Elodea canadensis* and ≥ 22.1 µg a.s./L for all the others). However, the experts agreed not to neglect the effects on *Charophyta*, since it is a non-potted species and the macrophytes provide habitat structure to many other species. Therefore, a data gap was identified to perform a toxicity study on *Charophyta* addressing the relative sensitivity.

Depending on the outcome of this study:

If the sensitivity of *Charophyta* is confirmed, the microcosm study can be used only as information that the first-tier endpoints might not be conservative enough;

If the sensitivity of *Charophyta* is not confirmed, the endpoint to be used for risk assessment should be the NOEC of 2.43 µg a.s./L (maximum measured concentration) for *Elodea canadensis*, with a safety factor of 2-5. A safety factor of 1 was not recommended by the experts, due to several uncertainties in the study (see above).

Outdoor field study on primary productivity and macrophytes/**Algae**:

The RMS proposed a NOEC for algae of 83.7 µg a.s./L based on chlorophyll and biomass. However, the experts noted that from the principal response curve (PRC) the NOEC for phytoplankton would be <0.4 µg a.s./L (nominal), while the NOAEC (including recovery) should be 48.32 µg a.s./L (maximum measured concentration of the nominal 83.7 µg a.s./L exposure).

Algae recover more easily than macrophytes, however, the time needed for recovery in the study was long (8 weeks), and the study does not take into account the multiple applications. Therefore, it was uncertain that recovery in the field would occur within a reasonable time (8 weeks after the first application). Consequently, also for algae, the meeting concluded that the NOEC should be used instead of an endpoint based on recovery. The NOAEC of 48.32 µg a.s./L may be used only in case of single application.

For the supported use (4 applications), the NOEC for algae could not be determined. Algae were more sensitive in the first-tier studies than *Lemna,* and both showed a higher sensitivity in the outdoor microcosm field study than the first-tier studies. Therefore, EFSA noted, after the PRAPeR 68 experts' meeting that it could be necessary to further address the effects of the formulation identified on algae in the outdoor microcosm field study. In this case the data gap identified at the PRAPeR 68 experts' meeting to provide a new study with the formulation product and the less sensitive species *Pseudokirchneriella subcapitata*, could be considered not necessary.

In addition to the above issues, the experts underlined that, in the outdoor microcosm study, indirect effects on zooplankton were not sufficiently addressed. *Daphnia magna* only was tested under semi-static conditions in water samples taken from the microcosm between day 16 and 36; macro-invertebrates and zooplankton productivity was monitored only on day 62. Moreover, many plant species were not fully submerged and lenacil was a persistent substance in the water/sediment system (see section4.2.1).

Overall, due to the uncertainties in the available outdoor field study (i.e. the use of potted plants which does not address the competition, application late in the season, variability in measured concentration from the beginning of the study, NOEC not determined for *Charophyta* and algae, indirect effects on zooplankton not sufficiently monitored, many plant species not fully submerged, persistence of lenacil in water/sediment system), the risk assessment for algae and for macrophytes could not be finalised, even in a first-tier assessment, because standard studies showed a lower sensitivity than the higher-tier study. Therefore, member state experts agreed that the first tier TER calculations for algae and macrophytes performed by the RMS, should be deleted from the list of endpoints.

The outcome of the discussion on the outdoor microcosm study was:

To use a NOEC instead of NOAEC and to express it in maximum measured concentration. Only for algae and in case of single application it was agreed to use the NOAEC of 48.32 µg a.s./L.

To set a data gap for a toxicity study on *Charophyta* in order to define a NOEC for macrophytes to be used for risk assessment; depending on the outcome of this study, if the NOEC of 2.43 µg a.s./L for *Elodea canadensis* is confirmed, a safety factor of 2-5 should be used.

To set a data gap for further studies to address the effects of the formulation identified on algae (by PRC analysis) in the outdoor microcosm field study, which take account of multiple applications (data gap identified by EFSA after the experts' meeting and during the written procedure).

The risk for the metabolites IN-KE 121 and IN-KF 313 was assessed to be low.

5.3. Risk to bees

On the basis of available data (i.e. acute contact toxicity study with technical lenacil and acute/oral toxicity study with formulation product), the risk assessment to bees was low (HQs far below to the Annex VI trigger of 50).

5.4. Risk to other arthropod species

Studies with the formulated product on *Aphidius rhopalosiphi*, *Typhlodromus pyri*, *Aleochara bilineata* and *Chrisoperla carnea* were available, indicating a low toxicity to non-target arthropods. A low first-tier in-field and off-field risk was estimated according to ESCORT II (HQs below the Annex VI trigger of 2).

5.5. Risk to earthworms

Acute studies with technical lenacil, formulation product and the metabolites IN-KE 121 and IN-KF 313 and *Eisenia foetida* were submitted. Also a reproductive study with the product was available. No acute and chronic effects were observed at the highest tested concentrations. The TERs calculated in a first-tier risk assessment were above the Annex VI triggers, indicating a low risk to earthworms.

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

The RMS stated in the DAR that no studies on soil macro-organisms were necessary since the field DT_{90} of technical lenacil in soil was <100 d. However, in an experiment performed in Spain, the DT_{50} was 88 days and the DT_{90}=291 days. This study was considered an outlier by the RMS, but the PRAPeR experts' meeting 67 on fate and behaviour, agreed to consider it as valid (see section 4.1.2). Formally, a data gap should be identified to provide a further study on Collembola. Nevertheless, EFSA agreed with the RMS that further studies were not necessary, in view of the low effects on non-target organisms, earthworms, soil micro-organisms and non-target plants.

5.7. Risk to soil non-target micro-organisms

No effects of >25 % on soil respiration and nitrification were observed in tests with technical lenacil up to concentration of 10×PEC_{soil} (equivalent to an application rate of 5 kg a.s./ha), indicating a low risk to soil non-target micro-organisms for the representative uses evaluated.

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

Herbicidal effects of the formulation product 'Venzar 80 WP' on vegetative vigour and of the formulation product 'Venzar 500 SC' (acceptable surrogate of Venzar 80% WP) on emergence were investigated in tests with dicotyl and monocotyl plant species. The lowest ER_{50} values were observed for *Lycopersicon esculentus* ER_{50} = 427 g a.s./ha in the vegetative vigour test and for *Brassica napus* ER_{50} = 177.2 g a.s./ha in the emergence test. The TERs were above the Annex VI trigger, indicating a low risk for non-target plants.

5.9. Risk to biological methods of sewage treatment

Technical lenacil did not inhibit the respiration of activated sewage sludge at the maximum concentration tested of 100 mg a.s./L. The risk to biological methods of sewage treatment is considered to be low.

6. Residue definitions

6.1. Soil

Definition for risk assessment: lenacil, IN-KF 313, IN-KE 121, 'Polar B', 'Polars'

Definition for monitoring: lenacil, 'Polar B', 'Polars' (provisional, pending on the final assessment for the unknown metabolites)

6.2. Water

6.2.1. Ground water

Definition for exposure assessment: lenacil, IN-KF 313, IN-KE 121, 'Polar B', 'Polars', M1, M2, M3

Definition for monitoring: lenacil, IN-KF 313, 'Polar B', 'Polars', M1, M2, M3 (provisional, pending on the final assessment for IN-KF 313 and the unknown metabolites)

6.2.2. Surface water

Definition for risk assessment

in surface water: lenacil, IN-KF 313, IN-KE 121, 'Polar B', 'Polars'

in sediment: lenacil, IN-KF 313, IN-KE 121

Definition for monitoring: lenacil, 'Polar B', 'Polars' (provisional, pending on the final assessment for the unknown metabolites)

6.3. Air

Definition for risk assessment: lenacil

Definition for monitoring: lenacil

6.4. Food of plant origin

Definition for risk assessment: lenacil

Definition for monitoring: lenacil

Food of animal origin

Definition for risk assessment: not required for the notified use

Definition for monitoring: not required for the notified use

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

6.5.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
lenacil	Moderate to medium persistence Single first order DT_{50} 11-18 days (20°C, pF2 soil moisture) in laboratory experiments Single first order DT_{50} 18-88 days in field dissipation trials (EU)	Low risk was identified for earthworms
IN-KF 313	Moderate to very high persistence Single first order DT_{50} 3-444 days (20°C, pF2 soil moisture)	Low risk was identified for earthworms
IN-KE 121	Low to moderate persistence Single first order DT_{50} 4-11 days (20°C, pF2 soil moisture)	Low risk was identified for earthworms
'Polar B'	Data gap - No information available	No information available
'Polars'	Data gap - No information available	No information available

6.5.2. Ground water

Compound (name and/or code)	Mobility in soil	>0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
lenacil	Medium to high mobility K_{Foc} 75 to 254 mL/g	<u>FOCUS</u>: No 0 scenario from 9 (Pearl) <u>Lysimeter</u>: Not found in the lysimeter leachate	Yes	Yes	Yes

IN-KF 313	Low to high mobility[a] K_{Foc} 79 to 824 mL/g	<u>FOCUS</u>: Data gap - available information is non reliable[b] <u>Lysimeter</u>: Not found in the lysimeter leachate	No	No enough information is available	Yes
IN-KE 121	Very high mobility K_{Foc} 30.5 to 43.5 mL/g	<u>FOCUS</u>: No 0 scenario from 9 (Pearl) <u>Lysimeter</u>: No information	No	No enough information is available	Yes
'Polar B'	Data gap - No information available	Data gap - No information available	No information is available	No information is available	No information is available
'Polars'	Data gap - No information available	Data gap - No information available	No information is available	No information is available	No information is available
M1	Data gap - No information available	<u>FOCUS</u>: No information <u>Lysimeter</u>: Yes Maximum annual average concentration in leachate of lysimeter (a.s. equivalent) 0.256 µg/L	No information is available	No information is available	No information is available
M2	Data gap - No information available	<u>FOCUS</u>: No information <u>Lysimeter</u>: Yes Maximum annual average concentration in leachate of lysimeter (a.s. equivalent) 0.519 µg/L	No information is available	No information is available	No information is available

M3	Data gap - No information available	FOCUS: No information Lysimeter: Yes Maximum annual average concentration in leachate of lysimeter (a.s. equivalent) 0.273 µg/L	No information is available	No information is available	No information is available

(a): Determined in a narrow range of acidic soils. Data gap for new data in alkaline soil.
(b): Non reliable information indicated, that in geoclimatic regions represented by Piacenza FOCUS groundwater scenario, contamination of groundwater above the 0.1 µg/L limit, cannot be excluded

6.5.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
lenacil	Further information is necessary to address the risk for aquatic organisms.
IN-KF 313	Low risk was identified for the aquatic organisms.
IN-KE 121	Low risk was identified for the aquatic organisms.
‘Polar B’ (only for surface water)	No information was available.
‘Polars’ (only for surface water)	No information was available.

6.5.4. Air

Compound (name and/or code)	Toxicology
lenacil	Low acute toxicity by inhalation (LC > 5.12 mg/L/4 hour)

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

- The material quantified under "loss on drying" should be quantified by specific methods (relevant for all representative uses evaluated, data gap identified by PRAPeR 66 meeting (April 2009), date of submission unknown, refer to chapter 1).

- Accelerated storage stability test of the preparation (relevant for all representative uses evaluated, data gap identified by PRAPeR 66 meeting (April 2009), date of submission unknown, refer to chapter 1).

- Sprayability test (relevant for all representative uses evaluated, data gap identified by PRAPeR 66 meeting (April 2009), date of submission unknown, refer to chapter 1).

- Confirmatory method for the determination of residues in water (relevant for all representative uses evaluated, data gap identified by PRAPeR 66 meeting (April 2009), date of submission unknown, refer to chapter 1).

- Analytical methods for the determination of residues in air with a LOQ of at least 48 $\mu g/m^3$ (relevant for all representative uses evaluated, data gap identified by PRAPeR 66 meeting (April 2009), date of submission unknown, refer to chapter 1).

- Depending the outcome of the exposure assessment for groundwater contamination, an evaluation of the relevance of the metabolites following the guidance document on relevant metabolites (SANCO/221/2000) has to be completed (refer to chapter 4.1 and 4.2.2).

- Metabolism study on rotational crops taking into account possible phytotoxicity problems (relevant for all notified intended uses, data requirement identified in the PRAPeR 70 meeting (May 2009), date of submission unknown; refer to chapter 3.1.2).

- Identification of the unidentified 'Polar B' and 'polars'. Depending on the outcome of any information submitted, exposure assessments and risk assessment for these unidentified metabolites may be necessary (relevant for all representative uses evaluated; data gap identified by PRAPeR 67 meeting (April 2009); date of submission unknown; see section 4.1.1).

- New soil batch adsorption study in one soil for IN-KF 313 under environmentally relevant alkaline conditions (relevant for all representative uses evaluated; data gap identified by PRAPeR 67 meeting (April 2009); date of submission unknown; see section 4.1.3).

- Further characterisation of the unidentified transformation products M1, M2 and M3 found in the leachates of the lysimeter study (relevant for all representative uses evaluated; data gap identified by PRAPeR 67 meeting (April 2009); date of submission unknown; see section 4.1.3).

- New FOCUS PECgw simulations for IN-KF 313 by at least two FOCUS models (PEARL and either PELMO or PRZM) (relevant for all representative uses evaluated; data gap identified by EFSA based on the open point set by PRAPeR 67 meeting (April 2009); date of submission unknown; see section 4.2.2).

- A toxicity study on *Charophyta* in order to define a NOEC for macrophytes to be used for risk assessment; (data gap proposed at the PRAPeR 68 experts' meeting, relevant for all representative uses evaluated; see section5.2).

- Further studies on algae to address the effects of the formulation identified in the outdoor microcosm field study, which take account of multiple applications (data gap identified by EFSA during the written procedure, after the PRAPeR 68 experts' meeting; relevant for all representative uses evaluated; see section5.2).

CONCLUSIONS AND RECOMMENDATIONS

OVERALL CONCLUSIONS

The conclusion was reached on the basis of the evaluation of the representative uses as herbicide as proposed by the applicant which comprise foliar spraying to control broad-leaved weeds in sugar beet and fodder beet, in all EU countries, at maximum four applications, at maximum application rate per treatment of 0.5 kg a.s./ha, with interval between applications of 1-2 weeks.

The representative formulated product for the evaluation was 'Venzar 80 WP', a wettable powder (WP) containing 800 g/kg lenacil, registered under different trade names in Europe.

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 products are possible, however data gaps were identified for the determination of the accelerated storage stability and sprayability.

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

Adequate analytical methods are available to monitor lenacil residues in food/feed of plant origin. Following the finalization of the residue definition for monitoring for soil, surface water and ground water, data gaps might have to be set for methods capable of analysing for the compounds in the residue definitions. A data gap for a confirmatory method for the determination of residues of lenacil in water was identified and also a residue method for air is required with a LOQ of at least 48 $\mu g/m^3$.

In mammals, lenacil is not acutely toxic via oral, dermal or inhalation routes; it is not a skin or eye irritant or skin sensitiser. In the short-term toxicity studies the rats and dogs were the most sensitive species showing alterations in the liver and thyroid function: the relevant oral NOAELs are 40.6 mg/kg bw/day and 44 mg/kg bw/day (rats and dogs, respectively;13-week studies). Lenacil is unlikely to be genotoxic. Increased incidences of malignant mammary adenocarcinomas were observed in rats and considered to be of relevance for humans. In mice, increased incidences of lung single alveolar tumours (adenoma and carcinoma) were observed and were considered of equivocal relevance for humans. Based on mammary gland and lung tumours, the classification Carc. cat.3, R40 'Limited evidence of a carcinogenic effect' was proposed. The relevant NOAEL from the long-term toxicity and carcinogenicity studies is 12 mg/kg bw/day (rat study). No specific effect on the reproductive parameters was found in multigeneration studies with rats: the relevant parental NOAEL is 81.9 mg/kg bw/day, the offspring NOAEL is 1727 mg/kg bw/day and the reproductive NOAEL is 4300 mg/kg bw/day. Tested in developmental toxicity studies, lenacil did not cause malformations in the rat and rabbits: the relevant maternal NOAEL in both species is 1000 mg/kg bw/day; the relevant developmental NOAELs are 1000 and 4000 mg/kg bw/day in rat and rabbits respectively (highest dose level tested). The ADI of 0.12 mg/kg bw/day was derived from the chronic rat study applying a SF of 100. An ARfD was considered not needed. The AOEL of 0.4 mg/kg bw/day (rounded) was based on the 13-week rat study supported by the 13-week dog study with a safety factor of 100. The operator exposure was estimated to be below the AOEL even without the use of personal protective equipment (German Model) and with gloves during mixing and loading and application (UK POEM Model). Worker and bystander exposure were estimated to be below the AOEL.

The metabolism of lenacil was investigated in sugar beets. Besides lenacil, the metabolite IN-KC943 formed by hydroxylation in the 7 position of lenacil and its glucosides and non identified polar metabolites were found in sugar beet leaves. As the most prevalent residue found in sugar beet metabolism was lenacil, the following residue definition was proposed for monitoring and risk assessment for root crops: lenacil only. A sufficient data base of residue trials from Northern and Southern Europe was submitted to propose an MRL for sugar beet (roots). Metabolism studies on rotational crops are not available. Based on the DT_{90} values found for the degradation of lenacil in soil in field studies, the PRAPeR experts meeting decided that metabolism studies on rotational crops are necessary to support the notified use.

Dietary burden calculations showed intake of lenacil residues through sugar or fodder beet roots and leaves slightly above the trigger value of 0.1 mg/kg feed. The PRAPeR experts meeting concluded that the intake was probably overestimated. Therefore, the majority of experts agreed that livestock metabolism studies should not be required.

A chronic dietary intake estimate was carried out by the RMS. The TMDI was below 0.4% of the ADI for all considered consumer groups. An acute dietary intake estimate was not carried out as no ARfD was set.

The information available on the fate and behaviour in the environment was not sufficient to carry out an appropriate environmental exposure assessment at the EU level. There were unidentified soil metabolites or metabolite fractions, which were either major metabolites in laboratory studies (Polar B, polars) or exhibited high potential for leaching in a lysimeter study (M1, M2, M3).

The adsorption potential of the major soil metabolite IN-KF 313 was determined in appropriate batch adsorption/desorption experiments, however the range of the pH of the used soils was too narrow. New data are needed for this metabolite at least in one alkaline soil.

Although the available FOCUS calculations for PECsw/sed (including the PEC calculations performed by EFSA) was agreed to be used in the risk assessment, the simulations should be updated considering the agreed substance input parameters. For the applied for intended uses, the potential for groundwater exposure by the active substance and the metabolite IN-KE 121 above the parametric drinking water limit of 0.1 µg/L, is low. However, no agreed PECgw simulations are available for the metabolite IN-KF 313. These calculations are needed for the finalization of the assessment of the potential groundwater contamination.

The risk to non-target species (i.e. birds and mammals, bees, non-target arthropods, earthworms, soil macro- and micro-organisms, other non-target organisms, and biological methods for sewage treatment) was expected to be low, except for aquatic organisms. Algae and aquatic plants were the most sensitive organisms and the effects were further assessed in higher tier studies. In particular, an outdoor microcosm field study on primary productivity and macrophytes was considered valid. This study showed several deficiencies, but it indicated a potential higher sensitivity of macrophytes and algae than the first-tier studies, therefore the experts considered it relevant for risk assessment. The experts agreed to consider the NOEC, expressed as measured concentration, as the most appropriate endpoint from this study, to be used with a safety factor of 2-5. However, a NOEC could not be finalised either for macrophytes or algae, and consequently it was not possible to finalise the risk assessment. A data gap was identified to address the sensitivity of *Charophyta* (the most sensitive species found in the microcosm study) and of algae. These further data should allow to define the endpoint from the outdoor microcosm study to be used for risk assessment.

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

None.

ISSUES THAT COULD NOT BE FINALISED

- The potential groundwater contamination by unknown major soil metabolites 'Polar B' and 'Polars' (from laboratory incubations) and by three unidentified lysimeter leachate chromatographically resolved components, M1, M2 and M3 cannot be finalised.

- The potential groundwater contamination by the major soil metabolite IN-KF 313 cannot be finalised.

- The risk to algae and aquatic plants could not be finalised since, on the basis of the data available, it was not possible to identify an appropriate endpoint for risk assessment.

CRITICAL AREAS OF CONCERN

- Regarding the metabolites M1, M2 and M3, the available information from the lysimeter study indicated a high potential for leaching to groundwater. The potential groundwater contamination by unknown major soil metabolites 'Polar B' and 'Polars' cannot be finalised.
- Available, non-reliable estimations (FOCUS PECgw calculations) indicated that the contamination of groundwater by the major soil metabolite IN-KF 313 above the relevant trigger cannot be excluded.
- The risk to algae and aquatic plants could not be finalised, since it was not possible, on the basis of the available data to identify the most sensitive endpoint relevant for risk assessment of either the single or multiple use. The first-tier risk assessment was not considered relevant since both algae and macrophytes showed a higher sensitivity in the outdoor microcosm study.

REFERENCES

Belgium, 2007. Draft Assessment Report (DAR) on the active substance lenacil prepared by the rapporteur Member State, Belgium, in the framework of Directive 91/414/EEC, November 2007.

Belgium, 2009. Final Addendum to the DAR on lenacil, compiled by EFSA, July 2009.

EFSA (European Food Safety Authority), 2009. Peer Review Report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance lenacil, EFSA Journal 2009: volume(issue): 1326.

APPENDICES

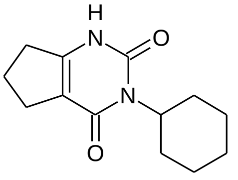
A. LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

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

Rapporteur Member State	Belgium
Co-rapporteur Member State	none

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	3-cyclohexyl-1,5,6,7-tetrahydrocyclopentapyrimidine-2,4(3H)-dione
Chemical name (CA) ‡	3-cyclohexyl-6,7-dihydro-1H-cyclopentapyrimidine-2,4(3H,5H)-dione
CIPAC No ‡	163
CAS No ‡	2164-08-1
EC No (EINECS or ELINCS) ‡	218-499-0 (EINECS)
FAO Specification (including year of publication) ‡	No FAO specification at time of evaluation
Minimum purity of the active substance as manufactured ‡	975 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	None
Molecular formula ‡	C13H18N2O2
Molecular mass ‡	234.3 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	Not applicable (cf. decomposition)
Boiling point (state purity) ‡	Not applicable (cf. decomposition)
Temperature of decomposition (state purity)	Decomposition starts at 270°C (99%)
Appearance (state purity) ‡	Fine powder, light beige (99%)
Vapour pressure (state temperature, state purity) ‡	1.7×10^{-9} Pa at 25 °C (99%)
Henry's law constant ‡	1.3×10^{-7} Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	99% pure: pH 5: 2.9 mg/L pH 7: 2.9 mg/L pH 9: 3.6 mg/L (all at 20°C)
Solubility in organic solvents ‡ (state temperature, state purity)	98.6% pure: Hexane: 1.3 mg/L Toluene: 80 mg/L Acetonitrile: 230 mg/L Ethylacetate: 500 mg/L Acetone: 690 mg/L Methanol: 1500 mg/L Dichloromethane: 2000 mg/L (All at 20° C)
Surface tension ‡ (state concentration and temperature, state purity)	62.5 mN/m (90% saturated solution, 24°C, 99%)
Partition co-efficient ‡ (state temperature, pH and purity)	99 % pure: pH 4 : Log Pow = 1.70 pH 7 : Log Pow = 1.69 pH 9 : Log Pow = 1.25 (All at 25° C)
Dissociation constant (state purity) ‡	pKa = 10.7 (99%)

UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	99% pure: <table><tr><td></td><td>λmax (nm)</td><td>ε (L.mol-1.cm-1)</td></tr><tr><td>Neutral water/acetonitrile 3 : 1 v/v</td><td>271 at λ = 290 nm</td><td>7880 1760</td></tr><tr><td>Acidic 0.133M HCl / acetonitrile 3 : 1 v/v</td><td>271 at λ = 290 nm</td><td>7990 1760</td></tr><tr><td>Alkaline 0.133M NaOH / acetonitrile 3 : 1 v/v</td><td>227 291</td><td>7220 10100</td></tr></table>
Flammability ‡ (state purity)	not highly flammable (98.6%)
Explosive properties ‡ (state purity)	not explosive (98.6%)
Oxidising properties ‡ (state purity)	not oxidising (98.6%)

Summary of representative uses evaluated for lenacil

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	kg as/hL min – max (l)	water L/ha min – max	kg as/ha min – max (l)		
Sugar beet Fodder beet (BEAVX)	Northern Europe, Southern Europe	Venzar 80 WP	F	Grass and Broad leaf weeds	WP	800 g/kg	Medium-low volume spraying, broadcast application	Post-emergence BBCH 10 (emergence first leaf) – 31 (beginning of crop cover)	1-4	7-14	0.03125 - 0.25	200-400	0,125 - 0,5	None *	Maximum of 0,5 kg a.s./ha per season [1] [2]

* A PHI value is not proposed. The product is applied early in the season according to the crop growth stage. In practice, there will normally be 90 to 120 days between the final application and harvest

[1]: It was not possible to finalize the risk assessment to aquatic organisms based on the data available.

[2]: Groundwater risk assessment not 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 situation should be described (e.g. fumigation of a structure) (b) Outdoor or field use (F), greenhouse application (G) or indoor application (I) (c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds (d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR) (e) GCPF Codes - GIFAP Technical Monograph No 2, 1989 (f) All abbreviations used must be explained (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench (h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated	(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).** (j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application (k) Indicate the minimum and maximum number of application possible under practical conditions of use (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha (m) PHI - minimum pre-harvest interval

Methods of Analysis

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

Technical as (analytical technique)	reversed-phase HPLC with UV detection
Impurities in technical as (analytical technique)	HPLC-DAD, ICP-OES, Karl Fischer
Plant protection product (analytical technique)	normal-phase HPLC with UV detection

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin	Lenacil
Food of animal origin	Not applicable (metabolism studies not required)
Soil	open
Water surface and drinking/ground	open
Air	Lenacil

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	HPLC-MS/MS, LOQ = 0.02 mg/kg (lenacil) (sugar beet leaf and root), ILV available
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not required, as currently no MRLs are requested
Soil (analytical technique and LOQ)	GC-MS, LOQ = 0.05 mg/kg (lenacil); HPLC-MS/MS, LOQ = 0.02 mg/kg (lenacil, IN-KF-313) open (pending finalization of the residue definition)
Water (analytical technique and LOQ)	HPLC-DAD, LOQ = 0.1 µg/L (lenacil) open (pending finalization of the residue definition) confirmatory method: open
Air (analytical technique and LOQ)	HPLC-MS/MS, LOQ = 0.1 mg/m³ (lenacil) open (cf. LOQ 0.48 µg/m3 is required)
Body fluids and tissues (analytical technique and LOQ)	Not required, as lenacil is not classified as toxic or highly toxic

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

	RMS/peer review proposal
Active substance	None

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

Rate and extent of oral absorption ‡	Rapid excretion (within 48h); Absorption: 85 % (based on urinary excretion and metabolites in the faeces (repeated low dose administration)
Distribution ‡	Uniformly distributed
Potential for accumulation ‡	No potential for accumulation (T1/2 =30 h)
Rate and extent of excretion ‡	Rapid and extensive (app. 95 %) within 48 h, mainly via urine (85 %) within 48 h, 12-19 % via faeces
Metabolism in animals ‡	Extensive metabolism by hydroxylation of cylcohexyl or cyclopentyl ring or both
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound and metabolites
Toxicologically relevant compounds ‡ (environment)	Parent compound and metabolites

Acute toxicity (Annex IIA, point 5.2)

Rat LD50 oral ‡	>5000 mg/kg bw	-
Rat LD50 dermal ‡	> 2000 mg/kg bw	-
Rat LC50 inhalation ‡	5.12 mg/L air /4h (nose only, aerosol)	-
Skin irritation ‡	Non- irritant	-
Eye irritation ‡	Non-irritant	-
Skin sensitisation ‡	Not sensitiser (M&K test)	-

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	White blood cells (rat, mice), thyroid and liver (rat, dog)	
Relevant oral NOAEL ‡	90-day mice: 157 mg/kg bw/d 90-day rat: 41 mg/kg bw/d 90-day dog: 44 mg/kg bw/d	-
Relevant dermal NOAEL ‡	No data, not required	-
Relevant inhalation NOAEL ‡	No data, not required	-

Genotoxicity (Annex IIA, point 5.4)	Overall no genotoxic potential

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

Target/critical effect ‡	Liver and thyroid (rat) lung (mice)
Relevant NOAEL ‡	12 mg/kg bw/d; 2-year, rat 332 mg/kg bw/d; 18-month mouse

Carcinogenicity ‡	Mammary gland tumour (rat), lung alveolar tumour, hepatocellular adenoma (mouse, equivocal relevance to humans)	**R40**

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Parental: effect on the thyroid Offspring: effect on the body weight gain Reproduction: no adverse findings	
Relevant parental NOAEL ‡	81.9 mg/kg bw/d	
Relevant reproductive NOAEL ‡	4300 mg/kg bw/day	
Relevant offspring NOAEL ‡	1727 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Maternal: rabbit: clinical signs and bw changes rat: no critical effect Developmental: no critical effect (rat and rabbits)	
Relevant maternal NOAEL ‡	Rat: 1000 mg/kg bw/day (highest dose tested) Rabbit 1000 mg/kg bw/d	
Relevant developmental NOAEL ‡	Rat: 1000 mg/kg bw/day (highest dose tested) Rabbit 4000 mg/kg bw/d (highest dose tested)	

Neurotoxicity (Annex IIA, point 5.7) lenacil

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

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Investigation of thyroid toxicity: NOAEL = 41 mg/kg bw/d (perchlorate discharge test in rats, no effect on the uptake and organification of iodine)
Studies performed on metabolites or impurities ‡	No studies provided

Medical data ‡ (Annex IIA, point 5.9) lenacil

	No reports of adverse effects and/or poisoning under work place conditions or under experimental agricultural use.

Summary (Annex IIA, point 5.10)	Value	Study	Safety

			factor
ADI ‡	0.12 mg/kg bw/d	Rat, long-term study	100
AOEL ‡	0.40 mg/kg bw/d	90-d rat study, supported by the 90d dog study	100
ARfD ‡	-	Not required	-

* No correction for oral absorption is required

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (e.g. name 50 % EC)	1% (concentrate) and 15.5% for the dilution in vitro (human skin)

Exposure scenarios (Annex IIIA, point 7.2)

Operator	The estimated exposure to Venzar 80 WP; field crop tractor mounted equipment; (application rate 200 L/ha; 500 g a.s./ha): -According to the UK model Without PPE: 104%f AOEL PPE (gloves): 33%of AOEL -According to the German model Without PPE: 16%of AOEL PPE (gloves): 12% of AOEL
Workers Bystanders exposure to lenacil	According to the Lloyd and Bell model: 0.23% of AOEL
Bystanders Workers exposure to lenacil	According to the BBA model: 4.8% of AOEL

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

	RMS/peer review proposal
Substance classified	Carc. Cat. 3; Xn;R40

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

Plant groups covered	Root crops (Sugar/fodder beets) – Foliar application
Rotational crops	Data gap: Based on the findings and information currently available residues in rotational crops should be addressed by a complete study taking into account possible phytotoxicity problems.
Metabolism in rotational crops similar to metabolism in primary crops?	Open
Processed commodities	Processing studies were not required
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not relevant
Plant residue definition for monitoring	Lenacil
Plant residue definition for risk assessment	Lenacil
Conversion factor (monitoring to risk assessment)	Not applicable

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

Animals covered	Not required.
Time needed to reach a plateau concentration in milk and eggs	-
Animal residue definition for monitoring	-
Animal residue definition for risk assessment	-
Conversion factor (monitoring to risk assessment)	-
Metabolism in rat and ruminant similar (yes/no)	-
Fat soluble residue: (yes/no)	No (log Po/w= 1.70)

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

	On the basis of the results of the metabolism study on rotational crops (data gap) it should be decided if field studies on rotational crops are necessary.

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

	Lenacil can be considered as stable under frozen storage conditions in sugar beet leaves and roots for at least 254 days (8,5 months).

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

A metabolism study in ruminants only is required.

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	Yes, according to guidance doc.7031/VI/95 -Dairy cattle: 0.105 mg/kg diet -Beef cattle: 0.135 mg/kg diet	No	Yes, according to guidance doc.7031/VI/95 0.12 mg/kg diet
Potential for accumulation (yes/no):	No	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No -No residues expected in ruminant matrices, -Lenacil not fat soluble	-	No -No residues expected in pig matrices, -Lenacil not fat soluble
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	-	-	-
Liver	-	-	-
Kidney	-	-	-
Fat	-	-	-
Milk	-		
Eggs		-	

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)
Sugar beet	Northern Europe	Roots: 4 x <0.02 mg/kg Leaves: 3x<0.02, 0.04 mg/kg	-	0.02* mg/kg (roots)	<0.02 mg/kg (roots) 0.04 mg/kg (leaves)	<0.02 mg/kg (roots and tops)
	Southern Europe	Roots: 3 x < 0.02 mg/kg Leaves: 2 x < 0.02; 0.03 mg/kg	-		<0.02 mg/kg (roots) 0.03 mg/kg (leaves)	<0.02 mg/kg (roots and tops)

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

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

ADI	0.12 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	0.023 % of ADI 0.4 % of the ADI (UK toddler) –EFSA PRIMo.
TMDI (% ADI) according to national (to be specified) diets	German child (3-5 years old): < 0.01% of ADI <0.2% of ADI for all the UK consumer categories.
IEDI (WHO European Diet) (% ADI)	Not applicable
NEDI (specify diet) (% ADI)	Not applicable
Factors included in IEDI and NEDI	Not applicable
ARfD	Not allocated
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	
Processing studies not required.				

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

Sugar/fodder beet (roots)	0.02* mg/kg

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

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

Mineralization after 100 days	47.6 to 61.1% after 120 days (reported as volatiles), [4,7a-14C2]-lenacil, (n = 5)
Non-extractable residues after 100 days	19.4 to 25.8% after 120 days [4,7a-14C2]-lenacil, (n = 5)
Metabolites requiring further consideration - name and/or code, % of applied (range and maximum)	IN-KE121–max.9.2 to 13.9% AR at 14 to 30 days (n = 4) IN-KF313–max.8.5 to 14.7% AR at 7 to 14 days (n = 4) 'Polar B'–max.6.8 to 14.6% AR at 60 to 91 days (n = 4) 'Polars'–max.12.5% AR at 120 days (n = 1, at 10°C)

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

Anaerobic degradation	
Mineralization after 100 days	No data, not required
Non-extractable residues after 100 days	No data, not required
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No data, not required reinforce
Soil photolysis	
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None

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

Laboratory studies

Parent	Aerobic conditions in EU soils						
Soil type	Organic C	pH ($CaCl_2$)	t °C/% MWHC	DT_{50}/DT_{90} (days)	DT_{50} (days) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Speyer 2.2 sandy loam	2.3	5.8	20°C/40%	15/50	15	0.983	1st order non linear regression
Sheringham sandy silt loam	1.2	5.4	20°C/40%	25/83	18	0.995	
Whimple clay loam	3.3	6.4	20°C/40%	14/46	14	0.988	

Wick loamy sand	1.0	5.6	20°C/40%	15/50	15	0.999	
Wolston sandy loam	1.8	6.0	20°C/40%	11/37	11	0.998	
Geometric mean					14.4	-	-

IN-KF313		Aerobic conditions						
Soil type	Organic C	pH	t °C/soil moisture	DT_{50} (days)	DT_{50} (days) 20°C pF2/10kPa	St. (r^2)	ff	Method of calculation
Sandy loam	0.58	6.3[1]	25°C/0.33 bar	350	440		-	1st order non linear regression
Sandy loam	0.52	6.4[1]	25°C/0.33 bar	237	298		-	
Silt loam	1.39	6.8[1]	25°C/0.33 bar	263	336		-	
Speyer 2.2 sandy loam	2.3	5.8[2]	20°C/40% MWHC	20	20	-	0.1398	
Sheringham sandy silt loam	1.2	5.4[2]	20°C/40% MWHC	18	13	0.995	0.5486	
Wick loamy sand	1.0	5.6[2]	20°C/40% MWHC	19	19	0.997	0.4085	
Whimple clay loam	3.3	6.4[2]	20°C/40% MWHC	3	3		0.7359	
Wolston sandy loam	1.8	6.0[2]	20°C/40% MWHC	12	12	0.996	0.3627	
geometric mean					40.9	-		-

[1]: in KCl
[2]: in $CaCl_2$

IN-KE121		Aerobic conditions in EU soils						
Soil type	Organic C	pH	t °C/% MWHC	DT_{50}/DT_{90} (days)	DT_{50} (days) 20°C pF2/10kPa	St. (r^2)	ff	Method of calculation
Speyer 2.2 sandy loam	2.3	5.8	20°C 40% MWHC	4.0	4.0	-	0.6687	1st order non linear regression
Wolston sandy loam	1.8	6.0	20°C 40% MWHC	6.2	6.2	0.995	0.4015	

IN-KE121		Aerobic conditions in EU soils					
Soil type	Organic C	pH	t °C/% MWHC	DT_{50}/DT_{90} (days)	DT_{50} (days) 20°C pF2/10kPa	St. (r^2)	ff	Method of calculation
Wick loamy sand	1.0	5.6	20°C 40% MWHC	10.5	10.5	0.997	0.4337	
Whimple clay loam	3.3	6.4	20°C 40% MWHC	4.7	4.7		0.5312	
Sheringham sandy silt loam	1.2	5.4	20°C 40% MWHC	12.3	8.9	0.996	0.3481	
Geometric mean					6.4	-		-

Field studies

Parent	Aerobic conditions								
Soil	Location	Organic C	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St (r^2)	DT_{50} (d) Norm.	Method of calculation
Silt Bare soil	France	0.71	6.1	10	25	84	0.832	Insufficient data to calculate	Non linear SFO
Silty sand Bare soil	Germany	0.56	5.4	10	28	91	0.841	Insufficient data to calculate	Non linear SFO
Loamy silt Bare soil	Germany	1.23	6.7	10	18	61	0.909	Insufficient data to calculate	Non linear SFO
Silty loam Bare soil	Spain	1.57	7.5	10	88	291	0.594	Insufficient data to calculate	Non linear SFO

pH dependence	None
Soil accumulation and plateau concentration	Not required

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n

Oshtemo	0.5	5.7	-	-	0.35	75	0.88
Sassafras	0.8	6.2	-	-	0.61	81	0.86
Traver	1.1	7.6	-	-	2.80	254	0.91
Bottom Watchley	3.6	5.2	-	-	7.87	219	0.94
Elmton	3.2	7.3	-	-	2.65	83	0.88
Wick	0.8	5.4	-	-	0.96	120	0.89
Wolston	1.9	6.0	-	-	1.49	78	0.90
Arithmetic mean					2.39	130	0.89
Median					1.49	83	0.89
pH dependence, Yes or No			No				

IN-KF313							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sassafras	0.5	6.4	-	-	4.3	824	0.69
Hillsdale	0.6	6.3	-	-	4.5	769	0.99
Tama	1.4	6.8	-	-	1.1	79	1.00
Arithmetic mean					3.3	557	0.89
pH dependence (yes or no)			No (however the range of soil pH is limited)				

IN-KE121							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Wick 285	1.0	5.6	-	-	0.435	43.5	0.92
Sheringham	1.0	6.4	-	-	0.404	40.4	0.96
Elmton	3.2	7.3	-	-	0.977	30.5	0.96
Arithmetic mean					0.61	38	0.95
pH dependence (yes or no)			No				

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

Column leaching	No data, not required
Aged residues leaching	No data, not required

Lysimeter/ field leaching studies	Location: Germany. Study type: 2 Lysimeters. Soil properties (0 to 30 cm): 76.4% sand, 20.3% silt, 3.6% clay, pH = 5.6, OC = 1.3%

Crop: Sugar beet

Dates of application, numbers of applications: Split application in year 1, with first application of 200 g a.s./ha on 5 June 1995 (BBCH 12-14) and second application of 300 g a.s./ha on 19 June 1995 (BBCH 16-18).

Duration: Four years

Average annual rainfall + irrigation (mm): 905, 939, 891 and 1085 mm, for the four years of the study

Average annual leachate volume (mm): For the duplicate lysimeters used in the test the total leachate values were 177.0/207.8, 350.9/377.4, 263.7/228.4 and 527.8/526.3 for the four years of the study (average value = 332.4).

Annual average concentrations in leachate:

Lenacil and the major soil metabolites IN-KF313 and IN-KE121 were not observed in any leachate during the four years of the study. Radioactivity in the leachate was composed of the following metabolites

Summary of first monitoring year

Lysimeter 1/1	**Mean conc in μg/L equiv a.s.**	**M1 (RT=3.08)**	**M2 (RT=3.52)**	**M3 (RT=8.16)**	**M4 (RT=9.46)**	**M5 (RT=14.08)**	**M6 (RT=4.28)**	**M7 (RT=11.56)**
Low [μg/L]		0.238	0.489	0.273	0.015	0.000	0.021	-
High [μg/L]	1.19	0.238	0.489	0.273	0.015	0.000	0.021	-
Lysimeter 1/2	**Mean conc in μg/L equiv a.s.**	**M1 (RT=3.08)**	**M2 (RT=3.52)**	**M3 (RT=8.16)**	**M4 (RT=9.46)**	**M5 (RT=14.08)**	**M6 (RT=4.28)**	**M7 (RT=11.56)**
Low [μg/L]		0.256	0.519	0.200	0.023	0.010	0.017	0.000
High [μg/L]	1.03	0.256	0.519	0.213	0.023	0.010	0.017	0.014

Summary of second monitoring year

Lysimeter 1/1	**Mean conc in μg/L equiv a.s.**	**M1 (RT=3.08)**	**M2 (RT=3.52)**	**M3 (RT=8.16)**	**M4 (RT=9.46)**
low [μg/L]		0.160 (0.164) [1]	0.080	0.091	0.032
high [μg/L]	0.46	0.169 (0.173) [1]	0.088	0.104	0.077 (0.080) [1]
Lysimeter 1/2	**Mean conc in μg/L equiv a.s.**	**M1 (RT=3.08)**	**M2 (RT=3.52)**	**M3 (RT=8.16)**	**M4 (RT=9.46)**
low		0.106	0.082	0.033	0.035

[µg/L]					
high [µg/L]	0.38	0.128 (0.131) 1	0.086	0.058	0.063

The mean concentrations of total AR in the leachate were 0.12-0.13 µg a.s. equivalent/L in 3rd year and 0.05 µg a.s. equivalent in 4th year

Radioactivity in soil monoliths at study termination

Amount of radioactivity in the soils at the end of the study = Total radioactivity in soil for the duplicate lysimeters was 13.2 and 11.8% AR which was present almost exclusively as a non-extractable bound residue. No analysis of extracts was performed as a result.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	DT_{50} (d): - Kinetics: - Field or Lab: -
Application data	Crop: sugar beet Depth of soil layer: 5 cm Soil bulk density: 1.5g/cm^3 plant interception: 20% crop interception Number of applications: 1 Interval (d): Application rate: 1 x 500 g a.s./ha

Lenacil $PEC_{(s)}$ (mg/kg)	Single application 1 x 500 g/ha Actual	Single application 1 x 500 g/ha Time weighted average
Initial	0.533	
Short term 24h 2d 4d	-	-
Long term 7d 14d 21d 28d 50d 100 d	-	-
Plateau concentration	Not relevant	

Metabolite IN-KE121 Method of calculation	Initial PEC values calculated from the initial parent PEC using the maximum observed in soil incubations and the ratio of the molecular weights. Molecular weight relative to the parent: 248.3/234.3 Max. observed: 13.9%
Application data	-

IN-KE121 $PEC_{(s)}$ (mg/kg)	Single application 1 x 500 g/ha Actual	Single application 1 x 500 g/ha Time weighted average
Initial	0.079	
Short term 24h 2d 4d	-	-
Long term 7d 14d 21d 28d 50d 100d	-	-
Plateau concentration	Not relevant	

Metabolite IN-KF313 Method of calculation	Initial PEC values calculated from the initial parent PEC using the maximum observed in soil incubations and the ratio of the molecular weights. Molecular weight relative to the parent: 248.3/234.3 Max. observed: 14.7%
Application data	-

IN-KF313 $PEC_{(s)}$ (mg/kg)	Single application 1 x 500 g/ha Actual	Single application 1 x 500 g/ha Time weighted average
Initial	0.083	
Short term 24h 2d 4d	-	-
Long term 7d 14d 21d 28d 50d 100 d	-	-
Plateau concentration	Not relevant	

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

Hydrolytic degradation of the active substance and metabolites > 10 %	pH 4: stable, DT_{50} > 1 year pH 7: stable, DT_{50} > 1 year pH 9: stable, DT_{50} > 1 year
Photolytic degradation of active substance and metabolites above 10 %	pH 5: stable, DT_{50} > 1 year
Quantum yield of direct phototransformation in water at Σ > 290 nm	The quantum yield (ϕ) for lenacil in pH5 aqueous buffer was 2.62×10^{-7}.
Readily biodegradable ‡ (yes/no)	Not biodegradable according to the criteria of OECD 301B.

Degradation in water / sediment

Lenacil	Distribution: Ruckhaltebecken - water phase, 92.8% at 0 days declining to 24.5% after ~120 days. Ruckhaltebecken - sediment phase, maximum 30.6% after 58 days. Schaephysen - water phase, 90.6% at 0 days declining to 5.5% after 120 days. Schaephysen – sediment phase, maximum 51.8% after 30 days.									
Water/sediment system	pH water phase	pH sed	t.°C	Deg rate whole sys. (days)	St. (r^2)	Deg rate water	St. (r^2)	Deg rate sed	St. (r^2)	Method of calculation
Ruckhalte-becken	8.3	7.5-7.6	20	DT_{50} - 122 DT_{90} - 405	-	-	-	-	-	1st order non linear regression
Schaephysen	7.9-8.0	7.0-7.1	20	DT_{50} - 103 DT_{90} – 342	-	-	-	-	-	
Geometric mean				DT_{50} – 112 DT_{90} - 372		-		-		

Metabolite IN-KF313	Ruckhaltebecken - water, max. 7.8% at ~120 days Ruckhaltebecken - sediment, max. 3% at 88 days Schaephysen - water, max 7.5% at ~88 days Schaephysen - sediment, max 10.7% at 120 days
Mineralization and non extractable residues	Ruckhaltebecken – CO_2 up to 3.8% after ~120 days. Schaephysen – CO_2 up to 4.8% after 120 days. Ruckhaltebecken – Non extractable residues up to 16.5% after ~120 days. Schaephysen – Non extractable residues up to 10.6% after 120 days.

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

Parameters used in FOCUSsw step 1 and 2	FOCUS Step 2 calculations for IN-KF 313 below was performed by EFSA after the meeting of experts PRAPeR 67. FOCUS software: Step 1 and 2 in FOCUS, version 1.1 Metabolite IN-KF313 Water solubility (mg/L): 261.8 mg/L

	Koc: 79 mL/g DT50 soil (d): 41 days DT50 water (d): 1000 days DT50 sediment (d): 1000 days DT50 system (d): 1000 days
	Application rate: 94.1 g/ha, calculated by: dose rate of the parent (500 g/ha) x MW correction factor (1.06) x maximum observed in w/s system (17.75%) No. of application: 1 Crop interception: minimal crop cover Crop: sugar beets Season of application: March-May

PEC of IN-KF 313 in surface water following a single application of 500 g a.s./ha (FOCUS Step 2)

FOCUS STEP 2 Scenario	Day after overall maximum	North Europe (application at March-May)			
		PECsw µg/L actual	PECsw µg/L TWA	PECsed µg/kg actual	PECsed µg/kg TWA
	0 h	5.0499	---	3.9664	---
	24 h	5.0208	5.0354	3.9637	3.9651
	2 d	5.0173	5.0272	3.9609	3.9637
	4 d	5.0104	5.0205	3.9555	3.9609
	7 d	5.0000	5.0140	3.9472	3.9568
	14 d	4.9758	5.0009	3.9281	3.9473
	21 d	4.9517	4.9885	3.9091	3.9377
	28 d	4.9277	4.9763	3.8902	3.9282
	42 d	4.8801	4.9522	3.8526	3.9093
	50 d	4.8531	4.9385	3.8313	3.8985
	100 d	4.6878	4.8542	3.7008	3.8321

FOCUS STEP 2 Scenario	Day after overall maximum	South Europe (application at March-May)			
		PECsw µg/L actual	PECsw µg/L TWA	PECsed µg/kg actual	PECsed µg/kg TWA
	0 h	9.2934	---	7.3165	---
	24 h	9.2614	9.2774	7.3114	7.3140
	2 d	9.2550	9.2678	7.3064	7.3114
	4 d	9.2421	9.2582	7.2962	7.3064
	7 d	9.2230	9.2472	7.2811	7.2988
	14 d	9.1783	9.2239	7.2458	7.2811
	21 d	9.1339	9.2013	7.2108	7.2635
	28 d	9.0897	9.1789	7.1759	7.2460
	42 d	9.0019	9.1345	7.1066	7.2110

FOCUS STEP 2 Scenario	Day after overall maximum	South Europe (application at March-May)			
		PECsw µg/L actual	PECsw µg/L TWA	PECsed µg/kg actual	PECsed µg/kg TWA
	50 d	8.9521	9.1093	7.0673	7.1912
	100 d	8.6472	8.9540	6.8265	7.0687

Parameters used in FOCUSsw step 3	Version control no.'s of FOCUS software: 'SWASH' (Surface Water Scenarios Help), version 1.1, incorporating: MACRO, FOCUS version 4.4.2, PRZM, FOCUS surface water version 1.5.6 and TOXSWA, FOCUS surface water version 2.4.2. <u>a.s.</u> Molecular weight (g/mol): 234.3. Water solubility (mg/L): 6 mg/L at 25°C. Vapour pressure: 2 x 10^{-7} Pa at 25°C. Median K_{OC} (mL/g): 83 1/n : 0.89 DT_{50} soil (d): 9.9 days. The proper value to be used in any calculations for further assessments is 14.4 days DT_{50} water (d): 1000 days worst-case default value. DT_{50} sediment (d): 123 days (representative worst case whole w/s system value used as a surrogate). Crop was-off factor: 0.03 cm^{-1} <u>Metabolite IN-KE121</u> Molecular weight: 248.3 Water solubility (mg/L): 1020 mg/L at 20°C Mean Koc: 38 mL/g 1/n: 0.94. The proper value to be used in any calculations for further assessments is 0.95 DT_{50} soil (d): 4.6 days. The proper value to be used in any calculations for further assessments is 6.4 days DT_{50} water/sediment system (d): 1000 days (worst-case value in the absence of water/sediment study data) DT_{50} water (d): 1000 days (worst-case value in the absence of water/sediment study data) DT_{50} sediment (d): 1000 days (worst-case value in the absence of water/sediment study data) Kinetic fraction (molar): 0.46 The proper value to be used in any calculations for further assessments is 0.48
Application rate	Number of applications: 1, 2 and 4 applications modelled Interval (d): 7 days Application rate(s): 1 x 500 g a.s./ha, 1 x 300 + 1 x 200 g a.s./ha and 4 x 125 g a.s./ha modelled with

	20% crop interception. Time of application (month or season): 7 days after emergence for the first application, emergence date is the FOCUS default for sugar beet in each location
Main routes of entry	Drainage, runoff and spray drift.

PEC of lenacil in surface water following a single application at 500 g a.s./ha seven days after emergence (FOCUS Step 3)

Crop was-off factor	0.03 cm^{-1}

Time (days)	Scenario/water body											
	D3		D4		D4		R1		R1		R3	
	Ditch		Pond		Stream		Pond		Stream		Stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max	2.621	--	0.109	--	2.172	--	0.139	--	2.405	--	2.551	--
1	1.298	2.065	0.107	0.108	0.002	0.142	0.137	0.138	0.001	0.948	0.005	2.120
2	0.175	1.346	0.106	0.107	0.002	0.072	0.136	0.137	<0.001	0.474	0.001	1.143
4	0.006	0.695	0.104	0.106	0.002	0.037	0.134	0.136	<0.001	0.237	<0.001	0.573
7	0.001	0.399	0.101	0.104	0.002	0.022	0.131	0.134	0.057	0.136	<0.001	0.328
14	<0.001	0.200	0.096	0.101	0.002	0.013	0.123	0.131	0.001	0.109	<0.001	0.164
21	<0.001	0.133	0.090	0.099	0.007	0.011	0.116	0.127	<0.001	0.075	<0.001	0.109
28	<0.001	0.100	0.087	0.096	0.013	0.010	0.110	0.124	<0.001	0.068	0.001	0.110
42	<0.001	0.067	0.079	0.092	0.004	0.010	0.098	0.117	<0.001	0.046	<0.001	0.073
50	<0.001	0.056	0.075	0.089	0.004	0.009	0.092	0.114	<0.001	0.039	<0.001	0.062
100	<0.001	0.028	0.055	0.077	0.002	0.006	0.062	0.102	<0.001	0.019	<0.001	0.031

Concentrations expressed in µg/L.

PEC of lenacil in surface water following two applications (300 g a.s./ha seven days after emergence followed by 200 g a.s./ha seven days later) (FOCUS Step 3)

Time (days)	Scenario/water body											
	D3		D4		D4		R1		R1		R3	
	Ditch		Pond		Stream		Pond		Stream		Stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max	1.365	--	0.086	--	1.124	--	0.131	--	2.643	--	3.567	--
1	0.674	1.074	0.085	0.086	0.002	0.075	0.129	0.130	0.001	1.042	0.941	3.087
2	0.091	0.700	0.085	0.085	0.002	0.038	0.128	0.129	<0.001	0.521	0.008	1.664
4	0.003	0.362	0.083	0.085	0.002	0.022	0.126	0.128	<0.001	0.261	0.002	0.834
7	0.001	0.207	0.081	0.084	0.765	0.020	0.124	0.127	0.063	0.162	0.001	0.477
14	0.002	0.173	0.076	0.081	0.002	0.016	0.116	0.123	0.001	0.120	<0.001	0.239
21	<0.001	0.115	0.074	0.079	0.009	0.013	0.110	0.120	<0.001	0.085	<0.001	0.174
28	<0.001	0.087	0.072	0.078	0.016	0.011	0.104	0.117	<0.001	0.070	<0.001	0.145
42	<0.001	0.058	0.065	0.075	0.005	0.011	0.092	0.110	<0.001	0.048	<0.001	0.097
50	<0.001	0.049	0.062	0.073	0.004	0.010	0.086	0.107	<0.001	0.040	<0.001	0.082
100	<0.001	0.024	0.045	0.064	0.002	0.006	0.059	0.093	<0.001	0.020	<0.001	0.041

Concentrations expressed in µg/L.

PEC of lenacil in surface water following 4 x 125 g a.s./ha applications at seven-day intervals, starting seven days after emergence (FOCUS Step 3)

Time (days)	Scenario/water body											
	D3		D4		D4		R1		R1		R3	
	Ditch		Pond		Stream		Pond		Stream		Stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max	0.441	--	0.065	--	0.375	--	0.284	--	4.892	--	5.217	--
1	0.255	0.360	0.064	0.064	0.002	0.032	0.282	0.283	0.005	2.528	1.376	4.515
2	0.050	0.250	0.064	0.064	0.002	0.017	0.279	0.282	0.001	1.265	0.012	2.433
4	0.002	0.132	0.063	0.064	0.002	0.014	0.275	0.280	0.090	0.633	0.003	1.257
7	<0.001	0.076	0.061	0.063	0.352	0.013	0.268	0.276	0.001	0.406	0.001	0.719
14	<0.001	0.071	0.058	0.061	0.006	0.012	0.253	0.269	0.529	0.212	<0.001	0.370
21	<0.001	0.048	0.055	0.060	0.010	0.009	0.240	0.267	<0.001	0.203	<0.001	0.254
28	0.198	0.052	0.053	0.058	0.354	0.008	0.227	0.264	<0.001	0.162	<0.001	0.195
42	<0.001	0.035	0.049	0.056	0.004	0.007	0.203	0.264	<0.001	0.114	<0.001	0.130
50	<0.001	0.038	0.046	0.055	0.003	0.007	0.191	0.262	<0.001	0.101	<0.001	0.112
100	<0.001	0.019	0.035	0.050	0.002	0.005	0.128	0.233	<0.001	0.051	<0.001	0.056

Concentrations expressed in µg/L.

PEC of lenacil in sediment following a single application at 500 g a.s./ha seven days after emergence (FOCUS Step 3)

Time (days)	Scenario/water body											
	D3		D4		D4		R1		R1		R3	
	Ditch		Pond		Stream		Pond		Stream		Stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max	0.575	--	0.220	--	0.093	--	0.292	--	0.408	--	0.660	--
1	0.430	0.548	0.220	0.220	0.034	0.053	0.292	0.292	0.171	0.283	0.374	0.563
2	0.315	0.493	0.220	0.220	0.027	0.042	0.292	0.292	0.129	0.221	0.282	0.471
4	0.225	0.398	0.220	0.220	0.022	0.033	0.292	0.292	0.097	0.169	0.213	0.369
7	0.173	0.318	0.219	0.220	0.019	0.028	0.292	0.292	0.086	0.134	0.169	0.296
14	0.123	0.235	0.218	0.220	0.016	0.027	0.290	0.292	0.149	0.114	0.125	0.222
21	0.100	0.194	0.217	0.219	0.017	0.026	0.287	0.292	0.088	0.112	0.103	0.187
28	0.085	0.169	0.217	0.219	0.028	0.026	0.283	0.291	0.070	0.104	0.090	0.165
42	0.066	0.138	0.215	0.219	0.024	0.024	0.275	0.290	0.052	0.090	0.072	0.137
50	0.059	0.126	0.215	0.218	0.023	0.024	0.272	0.290	0.046	0.083	0.064	0.126
100	0.033	0.086	0.210	0.217	0.016	0.021	0.245	0.282	0.026	0.060	0.036	0.091

Concentrations expressed in µg/kg.

PEC of lenacil in sediment following two applications (300 g a.s./ha seven days after emergence followed by 200 g a.s./ha seven days later) (FOCUS Step 3)

Time (days)	Scenario/water body											
	D3		D4		D4		R1		R1		R3	
	Ditch		Pond		Stream		Pond		Stream		Stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max	0.309	--	0.189	--	0.054	--	0.269	--	0.444	--	0.934	--
1	0.232	0.295	0.189	0.189	0.024	0.035	0.269	0.269	0.183	0.307	0.524	0.795
2	0.170	0.265	0.189	0.189	0.020	0.033	0.269	0.269	0.138	0.239	0.393	0.663
4	0.121	0.218	0.189	0.189	0.017	0.032	0.269	0.269	0.103	0.181	0.294	0.517
7	0.093	0.185	0.189	0.189	0.051	0.032	0.269	0.269	0.091	0.143	0.232	0.413
14	0.147	0.168	0.188	0.189	0.018	0.032	0.267	0.269	0.159	0.121	0.170	0.308
21	0.102	0.154	0.188	0.189	0.018	0.031	0.264	0.269	0.093	0.119	0.139	0.257
28	0.083	0.139	0.188	0.189	0.032	0.030	0.261	0.269	0.074	0.110	0.121	0.226
42	0.062	0.117	0.187	0.188	0.028	0.028	0.254	0.268	0.055	0.095	0.096	0.187
50	0.055	0.108	0.186	0.188	0.027	0.027	0.251	0.267	0.048	0.088	0.085	0.172
100	0.030	0.074	0.183	0.187	0.018	0.024	0.227	0.260	0.027	0.062	0.047	0.118

Concentrations expressed in µg/kg.

PEC of lenacil in sediment following four x 125 g a.s./ha applications at seven-day intervals, starting seven days after emergence (FOCUS Step 3)

Time (days)	Scenario/water body											
	D3		D4		D4		R1		R1		R3	
	Ditch		Pond		Stream		Pond		Stream		Stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max	0.154	--	0.158	--	0.033	--	0.632	--	0.927	--	1.353	--
1	0.128	0.150	0.158	0.158	0.026	0.028	0.632	0.632	0.411	0.688	0.758	1.148
2	0.105	0.140	0.158	0.158	0.025	0.027	0.632	0.632	0.310	0.542	0.623	0.957
4	0.083	0.122	0.158	0.158	0.023	0.025	0.632	0.632	0.279	0.412	0.442	0.761
7	0.069	0.104	0.158	0.158	0.022	0.025	0.631	0.632	0.224	0.343	0.346	0.611
14	0.054	0.083	0.158	0.158	0.021	0.024	0.628	0.632	0.637	0.269	0.251	0.456
21	0.045	0.081	0.158	0.158	0.019	0.023	0.623	0.631	0.204	0.277	0.204	0.381
28	0.110	0.075	0.158	0.158	0.018	0.023	0.619	0.631	0.162	0.253	0.187	0.336
42	0.051	0.071	0.157	0.158	0.017	0.022	0.608	0.628	0.151	0.229	0.145	0.280
50	0.044	0.070	0.157	0.158	0.016	0.021	0.601	0.627	0.128	0.215	0.128	0.257
100	0.023	0.056	0.148	0.158	0.013	0.018	0.554	0.614	0.068	0.154	0.070	0.176

Concentrations expressed in µg/kg.

PEC of IN-KE121 in surface water following a single application of lenacil at 500 g a.s./ha seven days after emergence (FOCUS Step 3)

Time (days)	Scenario/water body											
	D3		D4		D4		R1		R1		R3	
	Ditch		Pond		Stream		Pond		Stream		Stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max	<0.001	--	0.007	--	0.024	--	0.009	--	0.368	--	0.607	--
1	<0.001	<0.001	0.007	0.007	0.020	0.022	0.009	0.009	<0.001	0.145	0.159	0.526
2	<0.001	<0.001	0.007	0.007	0.017	0.021	0.008	0.009	<0.001	0.073	0.001	0.283
4	<0.001	<0.001	0.007	0.007	0.013	0.019	0.008	0.008	<0.001	0.036	<0.001	0.142
7	<0.001	<0.001	0.007	0.007	0.008	0.016	0.008	0.008	0.009	0.021	<0.001	0.081
14	<0.001	<0.001	0.007	0.007	0.004	0.011	0.008	0.008	<0.001	0.017	<0.001	0.040
21	<0.001	<0.001	0.006	0.007	0.005	0.009	0.007	0.008	<0.001	0.011	<0.001	0.027
28	<0.001	<0.001	0.006	0.007	0.004	0.008	0.007	0.008	<0.001	0.009	<0.001	0.020
42	<0.001	<0.001	0.006	0.007	0.002	0.006	0.006	0.007	<0.001	0.006	<0.001	0.014
50	<0.001	<0.001	0.006	0.006	0.002	0.006	0.006	0.007	<0.001	0.005	<0.001	0.011
100	<0.001	<0.001	0.005	0.006	0.001	0.004	0.004	0.006	<0.001	0.002	<0.001	0.006

Concentrations expressed in µg/L.

PEC of IN-KE121 in surface water following two applications of lenacil (300 g a.s./ha seven days after emergence followed by 200 g a.s./ha seven days later) (FOCUS Step 3)

Time (days)	Scenario/water body											
	D3		D4		D4		R1		R1		R3	
	Ditch		Pond		Stream		Pond		Stream		Stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max	<0.001	--	0.007	--	0.025	--	0.009	--	0.303	--	0.817	--
1	<0.001	<0.001	0.007	0.007	0.021	0.023	0.009	0.009	<0.001	0.119	0.214	0.707
2	<0.001	<0.001	0.007	0.007	0.018	0.022	0.009	0.009	<0.001	0.060	0.001	0.380
4	<0.001	<0.001	0.007	0.007	0.014	0.020	0.008	0.009	<0.001	0.030	<0.001	0.190
7	<0.001	<0.001	0.007	0.007	0.009	0.017	0.008	0.008	0.009	0.017	<0.001	0.109
14	<0.001	<0.001	0.007	0.007	0.004	0.012	0.008	0.008	<0.001	0.015	<0.001	0.054
21	<0.001	<0.001	0.007	0.007	0.006	0.009	0.007	0.008	<0.001	0.010	<0.001	0.036
28	<0.001	<0.001	0.007	0.007	0.004	0.008	0.007	0.008	<0.001	0.008	<0.001	0.027
42	<0.001	<0.001	0.006	0.007	0.002	0.007	0.006	0.007	<0.001	0.005	<0.001	0.018
50	<0.001	<0.001	0.006	0.007	0.002	0.006	0.006	0.007	<0.001	0.004	<0.001	0.015
100	<0.001	<0.001	0.005	0.006	0.001	0.004	0.004	0.006	<0.001	0.002	<0.001	0.008

Concentrations expressed in µg/L.

PEC of IN-KE121 in surface water following 4 x 125 g a.s./ha applications of lenacil at seven-day intervals, starting seven days after emergence (FOCUS Step 3)

Time (days)	Scenario/water body											
	D3		D4		D4		R1		R1		R3	
	Ditch		Pond		Stream		Pond		Stream		Stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max	<0.001	--	0.006	--	0.016	--	0.033	--	0.465	--	0.935	--
1	<0.001	<0.001	0.006	0.006	0.014	0.016	0.033	0.033	<0.001	0.240	0.246	0.810
2	<0.001	<0.001	0.006	0.006	0.012	0.015	0.033	0.033	<0.001	0.120	0.001	0.435
4	<0.001	<0.001	0.006	0.006	0.009	0.013	0.032	0.033	0.008	0.060	<0.001	0.218
7	<0.001	<0.001	0.006	0.006	0.006	0.011	0.031	0.032	<0.001	0.038	<0.001	0.125
14	<0.001	<0.001	0.006	0.006	0.003	0.008	0.030	0.031	0.038	0.020	<0.001	0.062
21	<0.001	<0.001	0.006	0.006	0.004	0.006	0.028	0.031	<0.001	0.017	<0.001	0.042
28	<0.001	<0.001	0.005	0.006	0.003	0.006	0.027	0.030	<0.001	0.014	<0.001	0.032
42	<0.001	<0.001	0.005	0.006	0.002	0.005	0.024	0.028	<0.001	0.013	<0.001	0.022
50	<0.001	<0.001	0.005	0.006	0.002	0.004	0.023	0.028	<0.001	0.011	<0.001	0.018
100	<0.001	<0.001	0.004	0.005	0.001	0.003	0.015	0.024	<0.001	0.006	<0.001	0.009

Concentrations expressed in µg/L.

PEC of IN-KE121 in sediment following a single application of lenacil at 500 g a.s./ha seven days after emergence (FOCUS Step 3)

Time (days)	Scenario/water body											
	D3		D4		D4		R1		R1		R3	
	Ditch		Pond		Stream		Pond		Stream		Stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max	<0.001	--	0.014	--	0.012	--	0.011	--	0.041	--	0.103	--
1	<0.001	<0.001	0.014	0.014	0.012	0.012	0.011	0.011	0.014	0.026	0.052	0.085
2	<0.001	<0.001	0.014	0.014	0.011	0.012	0.011	0.011	0.010	0.020	0.038	0.069
4	<0.001	<0.001	0.014	0.014	0.011	0.012	0.011	0.011	0.007	0.014	0.028	0.053
7	<0.001	<0.001	0.014	0.014	0.011	0.011	0.011	0.011	0.007	0.011	0.021	0.041
14	<0.001	<0.001	0.014	0.014	0.009	0.011	0.011	0.011	0.012	0.009	0.015	0.030
21	NC	<0.001	0.014	0.014	0.010	0.010	0.011	0.011	0.007	0.009	0.013	0.025
28	NC	<0.001	0.014	0.014	0.009	0.010	0.011	0.011	0.006	0.008	0.011	0.021
42	NC	<0.001	0.014	0.014	0.008	0.010	0.011	0.011	0.004	0.007	0.009	0.018
50	NC	<0.001	0.014	0.014	0.008	0.010	0.010	0.011	0.004	0.007	0.008	0.016
100	NC	<0.001	0.014	0.014	0.006	0.008	0.009	0.011	0.002	0.005	0.005	0.011

Concentrations expressed in µg/kg.
NC – Not calculable

PEC of IN-KE121 in sediment following two applications of lenacil (300 g a.s./ha seven days after emergence followed by 200 g a.s./ha seven days later) (FOCUS Step 3)

Time (days)	Scenario/water body											
	D3		D4		D4		R1		R1		R3	
	Ditch		Pond		Stream		Pond		Stream		Stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max	<0.001	--	0.015	--	0.012	--	0.011	--	0.033	--	0.137	--
1	<0.001	<0.001	0.015	0.015	0.012	0.012	0.011	0.011	0.012	0.021	0.069	0.113
2	<0.001	<0.001	0.015	0.015	0.012	0.012	0.011	0.011	0.008	0.016	0.051	0.092
4	<0.001	<0.001	0.015	0.015	0.012	0.012	0.011	0.011	0.006	0.012	0.037	0.070
7	<0.001	<0.001	0.015	0.015	0.011	0.012	0.011	0.011	0.006	0.010	0.029	0.055
14	<0.001	<0.001	0.015	0.015	0.010	0.011	0.011	0.011	0.012	0.008	0.021	0.040
21	NC	<0.001	0.015	0.015	0.011	0.011	0.011	0.011	0.006	0.008	0.017	0.033
28	NC	<0.001	0.015	0.015	0.010	0.011	0.011	0.011	0.005	0.007	0.015	0.029
42	NC	<0.001	0.015	0.015	0.009	0.010	0.011	0.011	0.004	0.006	0.012	0.024
50	NC	<0.001	0.015	0.015	0.008	0.010	0.011	0.011	0.003	0.006	0.011	0.022
100	NC	<0.001	0.015	0.015	0.007	0.009	0.009	0.011	0.002	0.004	0.006	0.015

Concentrations expressed in µg/kg.
NC – Not calculable

PEC of IN-KE121 in sediment following 4 x 125 g a.s./ha applications of lenacil at seven-day intervals, starting seven days after emergence (FOCUS Step 3)

Time (days)	Scenario/water body											
	D3		D4		D4		R1		R1		R3	
	Ditch		Pond		Stream		Pond		Stream		Stream	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max	<0.001	--	0.014	--	0.010	--	0.046	--	0.060	--	0.158	--
1	<0.001	<0.001	0.014	0.014	0.009	0.010	0.046	0.046	0.024	0.043	0.080	0.130
2	<0.001	<0.001	0.014	0.014	0.009	0.010	0.046	0.046	0.018	0.033	0.059	0.107
4	<0.001	<0.001	0.014	0.014	0.009	0.009	0.046	0.046	0.016	0.025	0.044	0.082
7	<0.001	<0.001	0.014	0.014	0.009	0.009	0.046	0.046	0.013	0.020	0.034	0.064
14	NC	<0.001	0.014	0.014	0.008	0.009	0.046	0.046	0.033	0.016	0.024	0.047
21	NC	<0.001	0.014	0.014	0.009	0.009	0.045	0.046	0.011	0.015	0.020	0.038
28	NC	<0.001	0.014	0.014	0.008	0.009	0.045	0.046	0.009	0.014	0.018	0.034
42	NC	<0.001	0.014	0.014	0.007	0.008	0.044	0.046	0.012	0.014	0.014	0.028
50	NC	<0.001	0.013	0.014	0.007	0.008	0.043	0.046	0.010	0.014	0.013	0.026
100	NC	<0.001	NC	0.014	0.006	0.007	0.037	0.045	0.005	0.011	0.008	0.018

Concentrations expressed in µg/kg.
NC – Not calculable

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUS gw modelling PEARL, FOCUS version 3.3.3
Application rate	Number of applications: 1 Interval (d): - Application rate: 1 x 500 g a.s./ha modelled with 20% crop interception. Time of application (month or season): 7 days after emergence, emergence date is the FOCUS default for sugar beet in each location

Used input parameters

Parameter	Lenacil	IN-KE121
Molecular weight	234.3	248.3
Vapour pressure	2 x 10^{-7} Pa at 25°C	1.51 x 10^{-7} Pa at 25°C
Water solubility	6 mg/L at 25°C	1020 mg/L at 20°C
K_{foc} (K_{fom})	83 (48)	38 (22)
1/n	0.88	0.95
DT_{50} (soil)	14.4 days	7.4 days*
Kinetic fraction	-	0.43*
Crop was-off factor	0.03 cm^{-1}	-

*: The proper values to be used in any calculations for further assessments were to be: soil DT_{50} 6.4 days, ff 0.48.

Scenario	80th percentile annual average concentration at 1 m depth (20 year simulation)	
	Lenacil	IN-KE121
Châteaudun	<0.001	0.012
Hamburg	<0.001	0.012
Jokioinen	<0.001	0.003
Kremsmünster	<0.001	0.006
Oakhampton	<0.001	0.010
Piacenza	0.009	0.040
Porto	<0.001	<0.001
Sevilla	<0.001	0.037
Thiva	<0.001	0.004

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

Direct photolysis in air	Not required
Quantum yield of direct phototransformation	Not required
Photochemical oxidative degradation in air	DT_{50} of 2.8 hours derived using the Atmospheric Oxidation Programme, Version 1.88 (Syracuse Research Corporation). OH radical concentration assumed to be 1.5 x 10^6 cm^{-3}
Volatilisation	Not studied.
	Not studied.
Metabolites	None

PEC (air)

Method of calculation	Expert judgement based on vapour pressure and Atkinson calculation.

$PEC_{(a)}$

Maximum concentration	Negligible.

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: lenacil, IN-KF 313, IN-KE 121, 'Polar B', 'Polars' Surface Water: lenacil, IN-KF 313, IN-KE 121, 'Polar B', 'Polars' Sediment: lenacil, IN-KE121 and IN-KF313 Ground water: lenacil, IN-KF 313, IN-KE 121,

	'Polar B', 'Polars', M1, M2, M3
Air:	lenacil

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

Soil (indicate location and type of study)	No data.
Surface water (indicate location and type of study)	A selective review of published literature on pesticide monitoring in surface waters was carried out. Martinez, R.C. et al (2000) analysed surface water and groundwater samples in 1998 from the Guarena and Almar river basins in Spain. No lenacil was found (detection limit <0.025 µg/L) in the 18 surface water and 23 groundwater samples analysed. Beernaerts, S. et al (2003) carried out a 2 year (1998-1999) monitoring study of the Dyle river in Belgium which is representative of a large part of the country. River water samples were taken each month from 8 sites. Peak concentrations of lenacil were less than 2 µg/L immediately after application and declined to undetectable within the next few sampling occasions. In summary, a water-monitoring programme in Spain reported that no lenacil was found in agricultural catchment areas while in Belgium transient lenacil residues were found in river water samples only at the time of application indicating point sources of contamination. <u>Conclusions:</u> Monitoring results are difficult to interpret because the pesticide use pattern, the pesticide use history, the climatic conditions are not known. These data are given as additional information.
Ground water (indicate location and type of study)	A selective review of published literature on pesticide monitoring in surface waters was carried out. Martinez, R.C. et al (2000) analysed surface water and groundwater samples in 1998 from the Guarena and Almar river basins in Spain. No lenacil was found (detection limit <0.025 µg/L) in the 18 surface water and 23 groundwater samples analysed.
Air (indicate location and type of study)	No data.

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

Candidate for R53

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 ‡				
Anas platyrhynchos	Lenacil	acute	**> 2000**	-
Colinus virginianus	Lenacil	acute	**> 2000**	-
Colinus virginianus	Lenacil	short-term	**> 1088**	> 5000
Colinus virginianus	Lenacil	long-term	**100.4**	1024
Mammals ‡				
rat	Lenacil	acute	> 5000	-
rat	Venzar 80 WP	acute	**> 4080 (a.s.)**	-
rat	Lenacil	long-term	**81.9**	1000
Additional higher tier studies ‡				
Not required.				

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

Crop and application rate : sugar/fodder beet, 1 x 0.500 kg a.s./ha

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
medium herbivorous	Acute	33.06	> 60.5	10
	Short-term	15.20	> 71.6	10
	long-term	8.06	12.4	5
small insectivorous	Acute	27.04	> 74.0	10
	short-term	15.08	> 72.1	10
	long-term	15.08	6.66	5
Tier 1 (Mammals)				
medium herbivorous	Acute	12.18	> 335	10
	long-term	2.97	27.6	5

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				
Oncorhynchus mykiss	lenacil	96 h (static)	Mortality, LC_{50}	**> 2.0 mg a.s./L** (mm)
Pimephales promelas	lenacil	96 h (static)	Mortality, LC_{50}	**> 2.0 mg a.s./L** (mm)
Cyprinus carpio	lenacil	96 h (semi-static)	Mortality, LC_{50}	> 3.1 mg a.s./L (mm)
Oncorhynchus mykiss	Venzar 80 WP	96 h (static)	Mortality, LC_{50}	**> 2.18 mg a.s./L** (mm) (exceeds water solubility)
Oncorhynchus mykiss	lenacil	21d (flow-through)	Growth, NOEC	2.3 mg a.s./L (mm)
Oncorhynchus mykiss	lenacil	90 d (flow-through)	Growth, NOEC	**0.16 mg a.s./L** (mm)
Aquatic invertebrate				
Daphnia magna	lenacil	48 h (static)	Mortality, EC_{50}	**> 8.4 mg a.s./L** (measured after 48 h)
Daphnia magna	Venzar 80 WP	48 h (static)	Mortality, EC_{50}	**> 2.93 mg a.s./L** (mm) (exceeds water solubility)
Daphnia magna	lenacil	21d (semi-static)	Reproduction, NOEC	**0.48 mg a.s./L** (mm)
Sediment dwelling organisms				
Not required.				
Algae				
Navicula pelliculosa	lenacil	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.036 mg a.s./L (mm) 0.096 mg a.s./L (mm)
Pseudokirchneriella subcapitata	lenacil	96 h (static)	Biomass: E_bC_{50} (72 h) Growth rate: E_rC_{50} (72 h)	**0.0077 mg a.s./L** (mm)[2] 0.016 mg a.s./L (mm)[2]
Pseudokirchneriella subcapitata	IN-KE 121	72 h (static)	Biomass: E_bC_{50} (72 h) Growth rate: E_rC_{50} (72 h)	**10.7 mg/L** (mm) 27.8 mg/L (mm)

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Pseudokirchneriella subcapitata	IN-KF 313	72 h (static)	Biomass: E_bC_{50} (72 h) Growth rate: E_rC_{50} (72 h)	**2.1 mg/L** (mm) 4.27 mg/L (mm)
Higher plant				
Lemna gibba	lenacil	7 d (semi-static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	**0.019 mg a.s./L** (mm)[2] 0.029 mg a.s./L (mm)[2]
[1] mm: mean measured concentration; nom: nominal concentration. [2] Endpoints were not considered relevant for first-tier risk assessment since both algae and macrophytes showed a higher sensitivity in the outdoor microcosm study.				
Microcosm or mesocosm tests				
Studies of the effects of the formulation Venzar 80 WP on populations of macrophytes, phyto- and zoo-plankton have been conducted in outdoor ditch microcosms. The applied concentrations (maximum measured concentrations in brackets) were 0.4 (< limit of detection), 1.53 (0.45), 5.81 (2.43), 22.1 (10.17) and 83.7 (48.32) µg a.s./L in a single application and the duration of the exposure was 98 days. Member state experts agreed to use maximum measured concentrations as valid endpoint. No significant adverse effects were observed for the periphyton productivity up to 48.32 µg a.s./L. For the phytoplankton community, the taxa showing the greatest adverse effects were *Cryptomonas*, *Nitzschia*, *Chlorella*, *Ankistrodesmus*, *Chlamydomonas* and *Tetraselmis*. A reduction in abundance compared to the control was observed for all treatment levels, but recovery was observed within 8 weeks, giving a NOAEC = 48.32 µg a.s./L. For the macrophyte community, no effects were observed at 48.32 µg a.s./L for *Sparganium erectum*, *Sagittaria sagittifolia*, *Myriophyllum proserpinacoides*, *Rorippa nasturtium-aquaticum* and *Veronica catenata*. At 10.17 µg a.s./L no effects were observed for *Alisma plantago-aquatica*, *Hottonia palustris*, *Ceratophyllum demersum*, *Lemna minor* and *Cladophora*. Statistically significant dose-related effects were observed in all treatments for *Charophyta*. No significant adverse effects were observed for the zooplankton and macro-invertebrates community up to 48.32 µg a.s./L. An overall **NOAEC = 10.17 µg a.s./L** was suggested, covering most of the species examined. The NOAEC can however not be used before the relative sensitivity of *Charaphyta* has been determined. Depending on the outcome of that study a NOEC should be determined with a safety factor of 2-5. In addition, effects on the most sensitive phytoplankton taking in to account multiple application should be addressed.				

Venzar 80 WP: formulation containing 83.0 % lenacil (measured), batch n° : DPX-B634-106
formulation containing 80.0 % w/w lenacil (nominal), batch n° : D2091011022
formulation containing 80.5 % w/w lenacil (measured), batch n° : NOV00HE037

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

FOCUS Step1

FOCUS Step 1 PEC_{SW} and PEC_{SED} estimates have not been reported.

FOCUS Step 2

FOCUS Step 2 PEC_{SW} and PEC_{SED} estimates have not been reported.

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Crop and application rate : sugar/fodder beet : 1 x 0.500 kg a.s./ha, 7 days after emergence

Test substance	Scena-rio[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg a.s./L)	Buffer zone distance	Max. PEC_{SW} [4] (µg a.s./L)	TER	Annex VI trigger[5]
lenacil	D 3	ditch	*O. mykiss*	96 h	> 2.0	1.3 m	2.621	> 763	100
Venzar 80 WP			*O. mykiss*	96 h	> 2.18			> 832	100
lenacil			*O. mykiss*	90 d	0.16			61.0	10
lenacil	D 3	ditch	*D. magna*	48 h	> 8.4	1.3 m	2.621	> 3205	100
Venzar 80 WP			*D. magna*	48 h	> 2.93			> 1118	100
lenacil			*D. magna*	21 d	0.48			183	10

Note: No risk assessment is provided for algae and macrophytes as the first tier endpoints are not protective enough.
[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 3.
[4] indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or twa values used
[5] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

Crop and application rate : sugar/fodder beet : 0.300 + 0.200 kg a.s./ha, first application 7 days after emergence and second application 7 days later

Test substance	Scena-rio[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg a.s./L)	Buffer zone distance	Max. PEC_{SW}[4] (µg a.s./L)	TER	Annex VI trigger[5]
lenacil	R 3	stream	*O. mykiss*	96 h	> 2.0	1.8 m	3.567	> 561	100
Venzar 80 WP			*O. mykiss*	96 h	> 2.18			> 611	100
lenacil			*O. mykiss*	90 d	0.16			44.9	10
lenacil	R 3	stream	*D. magna*	48 h	> 8.4	1.8 m	3.567	> 2355	100
Venzar 80 WP			*D. magna*	48 h	> 2.93			> 821	100
lenacil			*D. magna*	21 d	0.48			135	10

Note: No risk assessment is provided for algae and macrophytes as the first tier endpoints are not protective enough.

[1] drainage (D1-D6) and run-off (R1-R4)

[2] ditch/stream/pond

[3] include critical groups which fail at Step 3.

[4] indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or twa values used

[5] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

Crop and application rate : sugar/fodder beet : 4 x 0.125 kg a.s./ha, first application 7 days after emergence, subsequent applications at 7-day intervals

Test substance	Scena-rio[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg a.s./L)	Buffer zone distance	Max. PEC_{SW}[4] (µg a.s./L)	TER	Annex VI trigger[5]
lenacil	R 3	stream	*O. mykiss*	96 h	> 2.0	1.8 m	5.217	> 383	100
Venzar 80 WP			*O. mykiss*	96 h	> 2.18			> 418	100
lenacil			*O. mykiss*	90 d	0.16			30.7	10
lenacil	R 3	stream	*D. magna*	48 h	> 8.4	1.8 m	5.217	> 1610	100
Venzar 80 WP			*D. magna*	48 h	> 2.93			> 562	100
lenacil			*D. magna*	21 d	0.48			92.0	10

Note: No risk assessment is provided for algae and macrophytes as the first tier endpoints are not protective enough.

[1] drainage (D1-D6) and run-off (R1-R4)

[2] ditch/stream/pond

[3] include critical groups which fail at Step 3.

[4] indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or twa values used

[5] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

Metabolites

Crop and application rate : sugar/fodder beet : 1 x 0.500 kg a.s./ha, 7 days after emergence

Test substance	Scena-rio[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg a.s./L)	Buffer zone distance	Max. PEC_{SW}[4] (µg a.s./L)	TER	Annex VI trigger[5]
IN-KE 121	R 3	stream	*P. subcapitata*	72 h	10.7	1.3 m	0.607	17628	10
IN-KF 313	R 3	stream	*P. subcap-itata*	72 h	2.1	1.3 m	0.402	5224	10

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

Crop and application rate : sugar/fodder beet : 0.300 + 0.200 kg a.s./ha, first application 7 days after emergence and second application 7 days later

Test substance	Scena-rio[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg a.s./L)	Buffer zone distance	Max. PEC_{SW}[4] (µg a.s./L)	TER	Annex VI trigger[5]
IN-KE 121	R 3	stream	*P. subcapitata*	72 h	10.7	1.8 m	0.817	13097	10
IN-KF 313	R 3	stream	*P. subcap-itata*	72 h	2.1	1.8 m	0.431	4872	10

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

Crop and application rate : sugar/fodder beet : 4 x 0.125 kg a.s./ha, first application 7 days after emergence, subsequent applications at 7-day intervals

Test substance	Scena-rio[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg a.s./L)	Buffer zone distance	Max. PEC_{SW}[4] (µg a.s./L)	TER	Annex VI trigger[5]
IN-KE 121	R 3	stream	*P. subcapitata*	72 h	10.7	1.8 m	0.935	11444	10

Test substance	Scena-rio[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg a.s./L)	Buffer zone distance	Max. PEC_{SW} [4] (µg a.s./L)	TER	Annex VI trigger[5]
IN-KF 313	R 3	stream	*P. subcapitata*	72 h	2.1	1.8 m	0.350	6000	10

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

Mesocosm

Crop and application rate : sugar/fodder beet : 1 x 0.500 kg a.s./ha, 7 days after emergence.
The suggested NOAEC cannot be used before the relative sensitivity of *Charaphyta* has been determined. Depending on the outcome of that study, a NOEC should be determined with a safety factor of 2-5.

Crop and application rate : sugar/fodder beet : 0.300 + 0.200 kg a.s./ha, first application 7 days after emergence and second application 7 days later.
The suggested NOAEC cannot be used before the relative sensitivity of *Charaphyta* has been determined. Depending on the outcome of that study, a NOEC should be determined with a safety factor of 2-5. In addition, effects on the most sensitive phytoplankton taking in to account multiple applications should be addressed.

Crop and application rate : sugar/fodder beet : 4 x 0.125 kg a.s./ha, first application 7 days after emergence, subsequent applications at 7-day intervals.
The suggested NOAEC cannot be used before the relative sensitivity of *Charaphyta* has been determined. Depending on the outcome of that study, a NOEC should be determined with a safety factor of 2-5. In addition, effects on the most sensitive phytoplankton taking in to account multiple applications should be addressed.

Bioconcentration			
	lenacil	IN-KE 121	IN-KF 313
$logP_{OW}$	1.70 (pH 4 and pH 7); 1.25 at pH 9[1]	1.04[2]	1.04[2]
Bioconcentration factor (BCF)[1] ‡	Not required since all log P_{OW} values are < 3.0.		
1 Measured. 2 Predicted by WSKOWWIN V1.41 in US EPA EPISUITE.			

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)
lenacil ‡	-	> **25 µg a.s./bee**
Venzar 80 WP	> **100 µg a.s./bee**	> **100 µg a.s./bee**
Field or semi-field tests		
Not required.		

Venzar 80 WP : formulation containing 81.6 % w/w lenacil, batch n° : NOV00HE037

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

Crop and application rate : sugar/fodder beet, 1 x 0.500 kg a.s./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
lenacil	contact	< 20	50
lenacil	oral	-	50
Venzar 80 WP	contact	< 5.0	50
Venzar 80 WP	oral	< 5.0	50

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

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g/ha)
Typhlodromus pyri ‡	Venzar 80 WP	Mortality	> 2000 g a.s./ha
Aphidius rhopalosiphi ‡	Venzar 80 WP	Mortality	> 2000 g a.s./ha
Aleochara bilineata	Venzar 80 WP	Mortality	> 1000 g a.s./ha
Chrysoperla carnea	Venzar 80 WP	Mortality	> 1000 g a.s./ha

Venzar 80 WP : formulation containing 81.6 % lenacil, batch n° : NOV00HE037

Crop and application rate : sugar/fodder beet, 1 x 0.500 kg a.s./ha

Test substance	Species	Effect (LR_{50} g a.s./ha)	HQ in-field	HQ off-field[1]	Trigger
Venzar 80 WP	*Typhlodromus pyri*	> 2000	< 0.25	< 0.007	2
Venzar 80 WP	*Aphidius rhopalosiphi*	> 2000	< 0.25	< 0.007	2

[1] based on 2.77% drift deposition at 1 m from the treated area.

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, test substrate and duration	Dose (g a.s./ha)	Endpoint	% effect[a]	Trigger value
Aphidius rhopalo-siphi	adults	Venzar 80 WP, glass slides, 13 d	125 g a.s./ha, initial	Corrected mortality Reproduction	0.0 % 9.5 %	50 % 50 %
			250 g a.s./ha, initial	Corrected mortality Reproduction	2.9 % -	50 % 50 %
			500 g a.s./ha, initial	Corrected mortality Reproduction	5.0 % 13.6 %	50 % 50 %
			1000 g a.s./ha, initial	Corrected mortality Reproduction	0.0 % 15.5 %	50 % 50 %
			1500 g a.s./ha, initial	Corrected mortality Reproduction	0.0 % 18.4 %	50 % 50 %
			2000 g a.s./ha, initial	Corrected mortality Reproduction	27.5 % 42.9 %	50 % 50 %
Typhlodro-mus pyri	proto-nymphs	Venzar 80 WP, glass slides, 14 d	2000 g a.s./ha, initial	Corrected mortality Reproduction	-2.3 % 7 %	50 % 50 %
Aleochara bilineata	adults	Venzar 80 WP, quartz sand, 65 d	20 g a.s./ha, initial	Corrected mortality Reproduction	- 2.9 % 6.5 %	50 % 50 %
			500 g a.s./ha, initial	Corrected mortality Reproduction	- 5.9 % 7.88 %	50 % 50 %
			1000 g a.s./ha, initial	Corrected mortality Reproduction	0.0 % -0.1 %	50 % 50 %
Chrysoperla carnea	larvae	Venzar 80 WP, glass slides, 25 – 27 d	20 g a.s./ha, initial	Corrected mortality Reproduction	-5.6 % -60.0 %[b]	50 % 50 %
			500 g a.s./ha, initial	Corrected mortality Reproduction	-8.3 % -6.4 %[b]	50 % 50 %
			1000 g a.s./ha, initial	Corrected mortality Reproduction	-11.1 % -29.7 %[b]	50 % 50 %

a Corrected mortality: positive values = adverse effects; negative values = no adverse effects.
Effect on reproduction: negative values = adverse effects; positive values = no adverse effects.
b Based on reduction in viable eggs/female/day relative to control

Venzar 80 WP : formulation containing 81.6 % lenacil, batch n° : NOV00HE037

Field or semi-field tests
Not required.

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

Test organism	Test substance	Time scale	End point[1]
Earthworms			
Eisenia fetida	lenacil ‡	14 d	LC_{50} > 1000 mg a.s./kg soil d.w.
Eisenia fetida	IN-KE 121	14 d	LC_{50} > 1000 mg/kg soil d.w.
Eisenia fetida	IN-KF 313	14 d	LC_{50} > 1000 mg/kg soil d.w.
Eisenia fetida	Venzar 80 WP	56 d	NOER = 32.0 kg a.s./ha
Other soil macro-organisms			
Not required. The dissipation of lenacil and its metabolite IN-KF 313 was investigated at 4 different sites in Europe during 2001-2002 (Northern France, Germany and Spain). In all 4 trials lenacil was found only in the 0-10 cm layer. The metabolite IN-KF 313 was detected only in 2 trials and only in the 0-10 cm soil layer with residues below the limit of quantification. Under field conditions lenacil has DT_{50} values of 25, 28, 18 and 88 days and DT_{90} values of 84, 91, 61 and 291 days. The DT_{50} value of 88 days and the corresponding DT_{90} value of 291 days observed in the experiment performed in Spain can be considered as an outlier. This experiment is characterised by hot soil temperature (26 – 31 °C) and almost no precipitation during the first 3 months. Given that lenacil and its two major metabolites IN-KF 313 and IN-KE 121 do not persist in soil beyond 100 days and that the acute risks to earthworms, sensitive indicator species of non-target arthropods and soil microflora were shown to be acceptable, further studies on other soil non-target macro-organisms are not considered to be necessary.			
Soil micro-organisms			
Nitrogen mineralisation	lenacil	28 days	< 25 % effect at day 28 at application rates of 0.67, 3.33 and 6.67 mg a.s./kg soil d.w. (corresponding to 0.5, 2.5 and 5.0 kg a.s./ha)
Carbon mineralisation	lenacil	28 days	< 25 % effect at day 28 at application rates of 0.67, 3.33 and 6.67 mg a.s./kg soil d.w. (corresponding to 0.5, 2.5 and 5.0 kg a.s./ha)
Field studies			
Not required.			

Test organism	Test substance	Time scale	End point[1]

[1] Since the measured log P_{OW} of lenacil (1.70 at pH 4 and pH 7; 1.25 at pH 9) and the modelled log P_{OW} values for IN-KF 313 (1.04) and IN-KE 121 (1.04) are all less than 2.0, the toxicity endpoints for lenacil and its major soil metabolites may all be used directly without correction to compensate for the high organic matter content of the artificial soil used in the laboratory toxicity tests.

Venzar 80 WP : formulation containing 81.6 % lenacil, batch n° : NOV00HE037

Toxicity/exposure ratios for soil organisms

Crop and application rate : sugar/fodder beet, 1 x 0.500 kg a.s./ha

Test organism	Test substance	Time scale	Maximum PEC_{SOIL}	TER	Trigger
Earthworms					
Eisenia fetida	lenacil	14 d	0.533 mg a.s./kg soil d.w.	> 1876	10
Eisenia fetida	Venzar 80 WP	56 d	0.500 kg a.s./ha	64	5
Eisenia fetida	IN-KE 121	14 d	0.260 mg/kg soil d.w.	> 3846	10
Eisenia fetida	IN-KF 313	14 d	0.203 mg/kg soil d.w.	> 4926	10

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

Preliminary screening data

Not required.

Laboratory dose response tests; Crop and application rate : sugar/fodder beet, 1 x 0.500 kg a.s./ha

Most sensitive species	Test substance	ER_{50} (g a.s./ha) vegetative vigour	ER_{50} (g/ha) emergence	Exposure[1] (g a.s./ha)	TER	Trigger
Lycopersicon esculentum	Venzar 80 WP	427	-	13.9	30.7	5
Brassica napus	Venzar 500 SC[2]	-	177.2	13.9	12.7	5

[1] based on maximum single application at 500 g a.s./ha, 7 days post-emergence to sugar/fodder beet and 2.77% drift deposition at 1 m from the treated area.

[2] A suspension concentrate formulation containing 500 g lenacil/L. The effects of exposure to active substances distributed in soil are unlikely to be influenced by the co-formulants. Venzar 500 SC is therefore an acceptable surrogate for assessing the effects of lenacil on seedling emergence and development following applications of Venzar 80 WP.

Venzar 80 WP : formulation containing 81.6 % w/w/ lenacil, batch n° : NO00HE037
Venzar 500 SC : formulation containing 475 g/L lenacil, batch n° : 0870805 VI-NF1

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

Not required.

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

Test type/organism	Endpoint
Activated sludge	EC_{50} (3 h) > 100 mg a.s./L

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

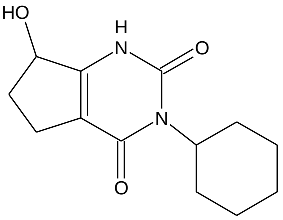
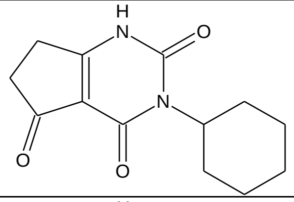
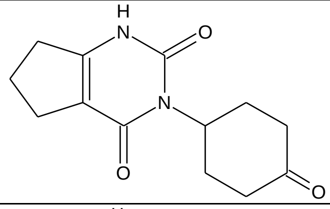
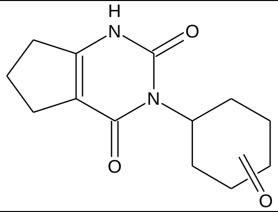
Compartment	
soil	Lenacil
water	Lenacil
sediment	lenacil
groundwater	none

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

	RMS/peer review proposal
Active substance	N, R50/53

	RMS/peer review proposal
Preparation	N, R50/53

B. USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name	Structural formula
IN-KC943	3-cyclohexyl-7-hydroxy-6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,5*H*)-dione	
IN-KF 313	3-cyclohexyl-6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4,5(3*H*)-trione	
IN-KE 121	3-(4-oxocyclohexyl)-6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,5*H*)-dione	
M15.0	3-(?-oxocyclohexyl)-6,7-dihydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,5*H*)-dione	

* The metabolite name in bold is the name used in the conclusion.

ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstract Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (formerly known as GIFAP)

GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level

OM	organic matter content
Pa	Pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year