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

clopyralid

finalised: 14 December 2005

SUMMARY

Clopyralid is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[1], as amended by Commission Regulation (EC) No 1490/2002[2]. This Regulation requires the European Food Safety Authority (EFSA) to organise a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

Finland being the designated rapporteur Member State submitted the DAR on clopyralid in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 2 December 2003. Following a quality check on the DAR, the peer review was initiated on 28 January 2004 by dispatching the DAR for consultation of the Member States and the sole applicant Dow AgroSciences. Two other companies (Barclay Chemicals and United Phophorus Ltd.) also notified but it was not possible to reach an agreement. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting in September 2004. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in January – March 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 29 September 2005 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as herbicide as proposed by the applicant which comprises broadcast spraying to control a narrow spectrum of broad-leaved weeds in cereals, oilseed rape, sugar beet and pasture at application rate up 127 g clopyralid per hectare for cereals, up to 300 g for oilseed rape and sugar beet, and up to240 g for pasture. Clopyralid can be used only as herbicide.
The representative formulated product for the evaluation was "Lontrel 100", an emulsifiable concentrate (SL), registered under different trade names in Europe.

[1] OJ No L 53, 29.02.2000, p. 25
[2] OJ No L 224, 21.08.2002, p. 25

Adequate methods are available to monitor all compounds given in the respective residue definition, except for food of animal origin.
Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.
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.

Clopyralid is rapidly and nearly completed absorbed in the rat. It is widely distributed and the highest concentration was found in the liver. There was no evidence of accumulation. Clopyralid is not metabolised. The acute toxicity is low i.e. oral LD_{50} > 5000 mg/kg bw, dermal LD_{50} > 2000 mg/kg bw and inhalatory exposure LC_{50} > 1 mg/L air. It does not induce skin irritancy or sensitization. However, clopyralid induced a marked irritation in the eyes of the rabbit and the symptoms persisted after 21 days. Thus, the proposal for classification for acute toxicity is Xi; R41"Risk of serious damage to eyes". It is not genotoxic, carcinogenic or toxic towards reproduction.
The acceptable daily intake (ADI) and acceptable operator exposure level (AOEL) is 0.15 and 1 mg/kg bw/day, with a safety factor of 100 applied. No ARfD is set.
A default of 10% for dermal absorption is set for Lontrel 100. The estimated operator exposure is below the AOEL even without PPE (34%), according to the UK POEM model.

No extensive metabolism occurred in the crops studied and hence clopyralid was found to be the major component of the residue in plants. The metabolism of clopyralid was similar in all studied crop groups and an adequate number of residue trials on the representative crops cereals, sugar beet, rape seed and pasture is available. For the use on cereals the experts' meeting for residues concluded that processing studies need to be submitted.
Significant amounts of clopyralid residues were found in potential feeding stuff. Therefore animal metabolism was investigated in ruminants and in poultry, indicating the majority of the residue found in animal matrices being clopyralid in free and conjugated form (the latter mainly in milk). From the study it was concluded that, apart from conjugation with glycin, clopyralid was not metabolised in livestock and that the occurrence of significant residues (>0.01 mg/kg) in edible animal tissues may be expected. Thus, feeding studies with clopyralid in ruminants, hens and pigs have been evaluated. It is noted that further data need to be submitted to assess the validity of some of the metabolism and feeding studies and to confirm the proposed MRLs for food of animal origin.
Data to support the assumption that no significant residues will occur in rotational crops have not been submitted, but may be required since there are indications that clopyralid residues in soil may be taken up and accumulated in rotational crops.
In a consumer risk assessment it was demonstrated that exposure to residues resulting from the representative uses of clopyralid is well below the ADI for the considered consumer groups. Even though intake of clopyralid residues is not likely to pose a high risk to consumers the current

assessment needs to be confirmed by the data still to be submitted. An acute risk for consumers through clopyralid residues on food is not anticipated, as no ARfD has been proposed.

No degradation products of clopyralid that accounted for more than 10 % AR were identified in soil under aerobic conditions. Volatiles collected in a trap with alkaline solution (attributed to CO_2) amounted up to a maximum of 83.3 % AR. Minimal degradation occurred under anaerobic conditions.

Photolysis will not contribute to the dissipation of clopyralid in soil. Clopyralid is moderate to medium persistent in soil under aerobic conditions at application rates in the range of the ones proposed for the representative uses but degradation seems to be slower when higher application rates are used.

In the field studies clopyralid dissipated slightly faster being low to moderate persistent. Only initial PEC soil are used in the ecotoxicological risk assessment.

The batch soil adsorption/desorption studies indicate that clopyralid is very high mobile in soil. Lysimeter studies show exceedance of 0.1 µg / L at individual data points but not as annual average. However, none of the lysimeter studies represent the worst case GAP. Notifier has indicated to the RMS their wish not to support anymore autumn uses. Therefore, neither interim nor final reports of the lysimeter study after the autumn application (Study K84) have been submitted. MS may need to require it for their assessment.

Clopyralid is expected to be stable to hydrolysis at environmental relevant pHs. Photodegradation will not be an environmental significant degradation pathway in water. Clopyralid should be classified as a non ready biodegradable.

Clopyralid partitions slowly from the water to the sediment and reaches a maximum of 30.6 % AR after 100 d into the sediment. There is practically no degradation of clopyralid in the water / sediment system and up to 91 % AR remains as clopyralid at the end of the experiment (100 d). Non extractable radioactivity in the sediment amounted up to 5.85 % AR at the end of the study. The amount of CO_2 formed slowly increased to between 2.3 % and 5.3 % AR after 100 d.

PEC sw were calculated based on the critical GAP from the table of representative uses and spray drift loadings. FOCUS sw was not used but run off and drainage were considered in the DAR. For run off PEC sw were calculated based on a 0.5 % run off from a 1 ha field to a 0.2 ha surface and 1m depth pond. For contamination through drain flow UK scheme was followed, giving rise to higher concentrations than those obtained by spray drift. This value was used for the risk assessment presented in the DAR. As for PEC sw, also drain flow PEC sed was the higher one. Therefore, EFSA proposes that a comprehensive aquatic risk assessment taking into account spray drift, run-off, drainage and the effectiveness of potential risk mitigation measures should be conducted following the FOCUS sw scheme to confirm the results of this assessment.

PEC gw of clopyralid were estimated using FOCUS-PELMO 2.2.2. and the mean normalized laboratory half life (DT_{50} = 38 d) corrected for the moisture content (36 d). Calculation of the 80th percentile of annual average concentrations of clopyralid at 1 m depth show that the 0.1 µg /L is exceeded for all the relevant scenarios corresponding to some of the proposed uses and for a number of scenarios of the rest of them. An assessment based on field half lives has been presented to the

RMS and summarized in addendum 2 (August 2005) but has not been peer reviewed. A complete report on this new modelling is required.

Based on the peer reviewed data, MS may need to consider risk for potential ground water contamination under vulnerable situations. Autumn uses are not longer supported by the notifier and are not covered by this assessment.

Concentration of clopyralid in the air compartment and transport through it is not expected to be significant.

The risk to terrestrial vertebrates, aquatic organisms, bees, non-target arthropods, earthworms and soil macro- and microorganisms from clopyralid used according to the proposed GAP is considered low based on available studies and information. For the maximum application rate proposed in a single application, 240 g a.s./ha for pasture, a 5 m buffer zone or drift reducing measures are necessary to protect non-target plants outside the field. Calculated TER values are 3.8 and 18.5 at 1 and 5 m distance respectively based on a spray drift of 2.77 %. No major soil or water/sediment metabolites were detected in the soil degradation studies or in the water/sediment studies. Therefore the risk assessment for the environment is based solely on clopyralid.

Key words: clopyralid, peer review, risk assessment, pesticide, herbicide

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BACKGROUND

Commission Regulation (EC) No 451/2000 laying down the detailed rules for the implementation of the second and third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC, as amended by Commission Regulation (EC) No 1490/2002, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Clopyralid is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating Finland as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, Finland submitted the report of its initial evaluation of the dossier on clopyralid, hereafter referred to as the draft assessment report, to the EFSA on 2 December 2003. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the revised version of the draft assessment report was distributed for consultation on 28 January 2004 to the Member States and the main applicant Dow AgroSciences as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed in an evaluation meeting on 27 September 2004 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier was attending this meeting.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised on behalf of the EFSA by the EPCO-Team at the Federal Office for Consumer Protection and Food Safety (BVL) in Braunschweig in January – March 2005. 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 with representatives from Member States on 29 September 2005 leading to the conclusions as laid down in this report.

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

In accordance with Article 8(7) of the amended Regulation (EC) No 451/2000, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

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

- the comments received
- the resulting reporting table (rev. 1-1 of 11 October 2004)
- the consultation report

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

- the reports of the scientific expert consultation
- the evaluation table (rev. 2-1 of 29 September 2005)

Given the importance of the draft assessment report including its addendum (compiled version of September 2005 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Clopyralid is the ISO common name for 3,6-dichloropyridine-2-carboxylic acid (IUPAC).

Clopyralid belongs to the class of pyridine herbicides such as fluroxypyr, picloram and trichlopyr. Clopyralid is taken up via leaves and roots and induces an epinastic response leading to chlorosis, cessation of normal growth and death.

The representative formulated product for the evaluation was "Lontrel 100", a soluble concentrate (SL), registered under different trade names in Europe. In the formulation the active substance is present as the olamine variant (2-hydroxyethylammonium).

The conclusion was reached on the basis of the evaluation of the representative uses as herbicide as proposed by the applicant which comprises broadcast spraying to control a narrow spectrum of broad-leaved weeds in cereals, oilseed rape, sugar beet and pasture at application rate up 127 g clopyralid per hectare for cereals, up to 300 g for oilseed rape and sugar beet, and up to 240 g for pasture. Clopyralid can be used only as herbicide.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of clopyralid as manufactured should not be less than 950 g/kg. At the moment no FAO specification exists.
The technical material contains no relevant impurities.

The assessment of the data package revealed no particular area of concern.
The main data regarding the identity of clopyralid and its physical and chemical properties are given in appendix 1.

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

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. clopyralid, its salts and conjugates in food of plant origin; clopyralid and its salts in soil and, water; clopyralid in air.
The methodology used is GC with EC or MS detection. A multi-residue method like the Dutch MM1 or the German S19 is not applicable to due the nature of the residues.
Due to the fact that the RMS had to re-evaluate the residues in food of animal origin (incl. proposal for residue definition, MRL and the enforcement methods (EPCO19, residues, February 2005), a final assessment of the enforcement methods was not possible. Due to the fact that EFSA has prepared an additional assessment (EFSA addendum residues, August 2005), the assessment of the analytical method given in the conclusion is rather based on this (see also 3.2 and 3.4).
Only one method can be regarded as suitable for enforcement purposes (Hastings, 2002b), because the other methods are using benzene. However, the validation extent is not in accordance with SANCO/825/00. In addition, the applicability of the method was not confirmed by an independent laboratory validation (ILV). Based on this, there is at the moment no adequate enforcement method for the determination of residue in food of animal origin available.

The discussion in the expert meeting (EPCO 20, March 2005) on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material and some clarification with respect to physical and chemical data as well as for analytical methods for the determination of residue.

2. Mammalian toxicology

Clopyralid was discussed at EPCO experts' meeting for mammalian toxicology (EPCO 18) in February 2005.

2.1 ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

Clopyralid is rapidly and nearly completed absorbed, based on urinary excretion data. The excretion is also rapid, >90% within 32 hours mainly in urine (both following oral and intravenous administration). It is widely distributed and the highest concentration was found in the liver. There was no evidence of accumulation. Clopyralid is not metabolised, since clopyralid is the only residue detected.

2.2 ACUTE TOXICITY

The acute toxicity is low i.e. oral LD_{50} > 5000 mg/kg bw as well as during dermal exposure > 2000 mg/kg bw and inhalatory exposure LC_{50} > 1 mg/L air (highest attainable concentration). It does not induce skin irritancy or sensitization. However, clopyralid induced a marked irritation in the eyes of the rabbit and the symptoms persisted after 21 days. The sensitizing properties were discussed at the experts´ meeting and a skin sensitization study in humans was presented in the addendum. However, the experts agreed that no classification was warranted.
Proposal for classification for acute toxicity is Xi; R41"Risk of serious damage to eyes".

2.3 SHORT TERM TOXICITY

The short term effects of clopyralid were studied in two 2-week and 13-week oral studies in the mouse and 28- and 90-day studies in the rat and a 13-day study in the rabbit as well as two studies in the dog, one 6-month study and one 1-year study.
The critical effects are haematological effects and an increase in the liver weight. The 90-day study was discussed in the experts´ meeting and the experts agreed to increase the NOAEL from 150 mg/kg bw/day to 1500 mg/kg bw/day since no histopathological changes were observed. The relevant oral NOAEL was agreed to be 100 mg/kg bw/day from the 1-year dog.
The relevant dermal NOAEL is > 1000 mg/kg bw/day No studies on repeated inhalation are required and available.

2.4 GENOTOXICITY

In the DAR the genotoxic properties of clopyralid were studied in a battery consisting of six *in vitro* studies and three *in vivo* studies. The studies were generally of old date and not all of them conducted according to GLP. However, the overall conclusion is that there is no genotoxic potential for, since all *in vitro* and *in vivo* tests were negative.

2.5 LONG TERM TOXICITY

Two rat and mouse long term toxicity studies were evaluated in the DAR. No major toxic effects were observed; at higher dose levels lesions in the gastric limiting ridge were observed in the rat (150 mg/kg bw/day). The gastric lesions were an issue for discussion in the experts´ meeting and the experts agreed that the finding was indeed adverse and confirmed the proposal on the NOAEL from the RMS. The overall NOAEL values for the mouse and rat is 500 mg/kg bw/day and 15 mg/kg bw/day, respectively.

2.6 REPRODUCTIVE TOXICITY

One multigeneration and one supplementary histopathology study in rat in order to determine the reproductive effects of clopyralid. The studies were not considered as acceptable by the RMS. The acceptability was discussed at the experts´ meeting and the experts concluded that the studies could be considered as acceptable since the highest dose was at least more than 700 mg/kg bw/day. Thus, the experts agreed that there were no direct effects on reproductive performance or fertility observed as well as to the offspring although it should be noted that the exact dose levels were not recorded.
The NOAEL for reproduction is > 1500 mg/kg bw/day, for offspring 500 mg/kg bw/day, and for parental 500 mg/kg bw/day.

In order to examine teratogenic or developmental effects of clopyralid one study in the rat and two studies in the rabbit were evaluated in the DAR. No adverse effects were observed at non-maternally toxic doses.
The NOAEL for maternal toxicity is 75 mg/kg bw/day and the NOAEL for developmental is > 250 mg/kg bw/day, in the rat.
The NOAEL for maternal and developmental toxicity in rabbit is 110 mg/kg bw/day

2.7 NEUROTOXICITY

No signs on neurotoxicity. No data on delayed neurotoxicity is available and not required since clopyralid does not belong to the family of organophosphates.

2.8 FURTHER STUDIES

Metabolites
There are no metabolites formed in the *in vivo* studies.

2.9 MEDICAL DATA

No detrimental effects on manufacturing personnel and no reported in the open literature on adverse effects reported.

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

ADI
The ADI is based on the NOAEL 15 mg/kg bw/day from the 2-year rat study, with a safety factor of 100 applied.
The ADI is 0.15 mg/kg bw/day.

AOEL

The AOEL is based on the NOAEL of 100 mg/kg bw/day from the 1-year dog study with a safety factor of 100. This was agreed on the experts´ meeting.

The AOEL is 1 mg/kg bw/day.

ARfD

Based on the low acute toxicity an ARfD was not considered necessary, which was agreed at the experts´ meeting

No ARfD is set.

2.11 DERMAL ABSORPTION

No dermal absorption studies were submitted by the applicant. The RMS proposed a default value of 10% for the formulation Lontrel 100 based on the properties of clopyralid where the Log P_{ow} is -2.63. The experts agreed with this proposal and 10% dermal absorption was considered for both concentrate and the diluted formulation.

2.12 EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Lontrel 100 is a SL (aqueous based soluble concentrate) containing 100 g clopyralid/L for use on broadleaf weeds in low crops.

Operator exposure

According to the intended uses submitted by the notifier the maximum applied dose is 0.2 kg clopyralid/ha, and the minimum volumes 80 L/ha using the tractor mounted boom with hydraulic nozzles.

The estimated operator exposure is below the AOEL even without PPE, according to the UK POEM model (work rate 50 ha/day), see table beneath.

Estimated exposure presented as % of AOEL (1 mg/kg bw/day), according to calculations with the UK POEM model. The default for body weight of operator is 60 kg.

Model	No PPE	With PPE
UK POEM	34%	4%

PPE (personal protective equipment): gloves during mixing and loading.

Worker exposure

The estimated worker exposure is below the AOEL, approximately < 4% of the AOEL.

Bystander exposure

The estimated acute exposure of a bystander is also below the AOEL (<1% of the AOEL).

3. Residues

Clopyralid was discussed at EPCO experts' meeting for residues (EPCO 19) in February 2005.

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

Plant metabolism was studied by applying clopyralid radio-labelled in two positions as a foliar spray to sugar beet, oilseed rape and cabbage at the intended application rate. The submitted study in pasture was not done in compliance with GLP and thus regarded by RMS as additional information only.

At maturity most of the radioactivity was taken up into the plants, the major radioactive compound was unchanged clopyralid, the anionic form (salt) and conjugated forms of clopyralid. Conjugated clopyralid was present at low levels in beet shoots (*ca* 1% TRR), but at levels 18-30% TRR in oilseed rape matrices. Together all clopyralid fractions accounted for 89 – 97 % of TRR. No other significant metabolites were detected.

In sugar beets clopyralid (including salts and conjugates) accounted for 0.36 and 0.38 mg/kg in beets and shoots, respectively. In oilseed rape, clopyralid fractions accounted for 0.71 mg/kg in straw and 0.06 mg/kg in seeds. In cabbage plants unchanged clopyralid was found to be the major component of the residue, accounting for 0.32 mg/kg in cabbage heads and 1.2 mg/kg in wrapper leaves. It was stated that the presence of residues in the cabbage hearts indicates translocation from the immature leaves with the residue level being diluted by growth. Based on the supportive study on pasture, the metabolism of clopyralid in grass is also very limited and the reduction of residue levels (from 13 mg/kg to 0.16 mg/kg) is due to the growth dilution.

No extensive metabolism occurred in the crops studied and clopyralid (including anionic form) was found to be the major component of the residue. However, depending on the crop clopyralid conjugates seem to build a major part of the residue, and furthermore, the analytical methods employed in recent supervised residue trials (Hastings, 2002) include a hydrolysis step covering potentially present conjugated forms of clopyralid as well. The method by Hastings is also the proposed enforcement method for food of plant origin. Therefore, the residue definition in plants should be clopyralid including its salt and conjugates, expressed as clopyralid for risk assessment and monitoring purposes. It is noted that the proposal for a plant residue definition agreed in the experts' meeting for residues was limited to clopyralid only, based on previous RMS information that no hydrolysis step was included in the relevant methods of analysis and on the view that, with the exception of rapeseed, the level of conjugates was negligible in the edible part of the crops studied. There is also indication from supervised residue trials (see below), that clopyralid (including salts) might be a valid alternative to define the residue in plants for monitoring purposes, provided that a validated enforcement method was available.

The metabolism of clopyralid was similar in all studied crop groups, thus the metabolic behaviour of clopyralid in plants can be regarded sufficiently studied. The proposed residue definition might apply for plants in general.

A range of supervised residue trials were conducted with clopyralid on cereals, sugar beet, rape seed and pasture at the critical GAP in northern and southern areas of Europe. Residues in the trials were determined as clopyralid. In most instances a hydrolysis step was included in the used analytical methods. Residues above the LOQ were found in all studied crops. In few trials from the 1970's on oilseed rape and sugar beets residues have been analysed with a method without a hydrolysis step. No significant differences in residue levels observed in those trials compared to the more recent residue trials in oilseed rape and sugar beets were observed. Hence those trials were included in the evaluation.

Processing studies were performed with rapeseed, and commercial sugar beet processing fractions have been monitored. No concentration of clopyralid was observed in oil samples. Clopyralid residues were concentrated during processing of sugar beet, but residue levels were below the limit of detection in refined sugar. For cereals no processing study was submitted. Therefore the experts' meeting for residues agreed on that such study has to be provided.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Studies on residues in succeeding crops have not been submitted because the persistence of clopyralid in soil was expected to be low to moderate on the basis of soil dissipation studies (see 4.1.2) and hence no significant residues of clopyralid were expected to remain in soil until sowing or planting of possible succeeding crops.

However, RMS and EFSA agreed on in the 2nd evaluation meeting that the following considerations need to be made: In laboratory studies with an application rate below the maximum intended rate, the $DT_{90\ lab}$ exceeded 100 days (up to 217 days, mean 113 days). Degradation seems even to be slower when higher application rates are used (see 4.1.2). Furthermore, metabolism studies indicated that clopyralid is systemically taken into plants and readily translocated in plants. Soil –plant transition factors to estimate the residue situation in rotational crops have been calculated by RMS and presented in the evaluation meeting. The values indicate that there might be good uptake from soil or even accumulation in the plants, and soil residues above 0.001 mg/kg might be present at the time of harvesting rotational crops. Therefore, further data may be required to support and corroborate the initial assumption that no significant residues will occur in rotational crops. It is noted that, since the above estimates were presented by RMS after the expert meeting and no addendum is available, the information was not peer reviewed.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Significant amounts of clopyralid residues were found in potential feeding stuff. Therefore animal metabolism was investigated in ruminants and in poultry. In these studies radio-labelled clopyralid was orally administered to lactating goats, to broiler chicken and laying hens. In addition the excretion of unlabelled clopyralid was investigated in lambs. It is noted that all of this studies are

from the 70's and early 80's and show partially significant deviations from the requirements of current applicable guidelines. The goat studies is lacking of the detailed experimental report. Thus, this report should be provided in order to assess the validity of the study.
The studies indicated that the majority of administered radioactivity was excreted as unchanged clopyralid by both species. Residues found in milk from goats consisted of about equal amounts of clopyralid and the glycine conjugate of clopyralid, which could be hydrolysed to clopyralid under alkaline conditions. In goat tissues conjugate levels were low or undetectable. The residues in tissues and eggs of hens were identified as unchanged clopyralid. Hence it was concluded that, apart from conjugation with glycin, clopyralid was not metabolised in livestock. A residue definition for food of animal origin was not proposed by RMS. Based on an evaluation of EFSA subsequent to the experts' meeting discussions the following proposal was made (EFSA addendum): Clopyralid including its salt and conjugates, expressed as clopyralid for risk assessment and monitoring purposes. Even though RMS agreed to the EFSA proposal, it is noted that the proposal was neither peer reviewed nor discussed by experts.

Arising from the evaluation of representative uses and livestock metabolism, it is expected that significant residues (>0.01 mg/kg) may occur in edible animal tissues when livestock is exposed to clopyralid residues in feed. Therefore, the residue behaviour of clopyralid was studied in dairy cattle, beef cattle, laying hens and pigs by feeding different concentrations of clopyralid in the diet comparable to, or exceeding, the estimated intake from ingesting treated pasture (dairy and beef cattle) or cereal grains and sugar beets (pigs, poultry). Again, it is noted that some one of the studies is lacking of the detailed experimental reports. Thus, these reports should be provided in order to assess the validity of the respective studies.
After exposure, residues disappeared rapidly. With chickens, residues were not detected at any of the feeding levels up to *ca* 10 mg/kg feed in any of the tissues examined. With pigs, the animal feeding studies showed that residues in pork products would not be detected at feeding levels of *ca* 100 mg/kg feed. In contrast, it could be concluded from a feeding study with calves that for cattle significant residues might be present in meat, liver, kidney and milk when exposed to the estimated maximum level of clopyralid residues. It is noted, that the findings for cattle are based on an evaluation of EFSA (EFSA addendum) and were contrary to the initial proposal of RMS, according to which no residues above 0.01 mg/kg are expected in bovine products and milk. However, in the 2nd evaluation meeting RMS basically agreed on the EFSA addendum and the proposed MRLs for food of animal origin. But again, it is noted that the proposal was not peer reviewed and moreover, that the data on processing of cereals still to be submitted might change the estimates of livestock dietary burden.

3.3. CONSUMER RISK ASSESSMENT

To assess the long-term dietary risk to consumers, TMDIs were calculated from the proposed MRLs for food of plant origin, based on the WHO standard European diet and the German diet. TMDIs were calculated to be 6 % of the ADI (WHO European diet - adults 60 kg) and 11 % of the ADI (German diet – female child 13.5 kg). In an intake assessment including the proposed MRLs for food of animal

origin it was demonstrated that the contribution to the ADI from consumption of animal products is less than 1% for an adult.
According to these results it is unlikely that the chronic intake of clopyralid residues will pose a high risk to consumers. Even though, it is noted that the exposure assessment cannot be conclusive unless the outstanding data on processing of cereals, on residues from crop rotation and on animal metabolism and feeding studies were submitted.

No ARfD was allocated for clopyralid. Thus, a short-term intake of clopyralid residues is unlikely to present a risk to consumers.

3.4. PROPOSED MRLS

On the basis of the results of supervised residue trials and livestock feeding studies, the following MRLs are proposed:

Food/feed of plant origin	
Cereals	2 mg/kg
Sugar beets	1 mg/kg
Rapeseed	0.1 mg/kg

To be confirmed by outstanding data, not peer reviewed:

Food/feed of animal origin	
ruminant kidney	0.5 mg/kg
ruminant meat, ruminant liver	0.1 mg/kg
fat, meat and offal except ruminant meat and offal	0.05* mg/kg
milk	0.02 mg/kg
eggs	0.05* mg/kg

4. Environmental fate and behaviour

Clopyralid was discussed on the experts' meeting on fate and behaviour in the environment EPCO 16 (January-February 2005).

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Clopyralid metabolism in soil under dark aerobic conditions at 20 °C was investigated in two studies with a total of six different soils. The six soils covered a range of pH (6.0-8.3), clay contents (3 % - 26 %) and organic matter content (1.28 % - 27.6 %). Additionally one of the soils was tested at 10 °C and at various moisture levels.
No degradation product was identified in the first study (five soils), likely due to the limitation of the analytical methodology employed (TLC). In the second study some unidentified radioactive regions

were separated by HPLC, none accounting for more than 10 % AR. Non extractable radioactivity increased to a maximum of 35 % AR after 92 d. Volatiles collected in a trap with alkaline solution amounted up to a maximum of 83.3 % AR. No identification of the volatiles was attempted and precipitation with $BaCl_2$ was performed only in one of the experiments (applicant claim not reported in the DAR but in the Reporting table). Based on complementary evidences such the soil volatilization study, it was accepted that most of the radioactivity found in the alkaline volatiles trap should be attributed to CO_2.

Degradation under dark anaerobic conditions at 20 °C was investigated in a study with a sandy clay loam soil. Analysis of soil and water by HPLC indicated that minimal degradation occurred under anaerobic conditions and no transformation products were found during the anaerobic experiment.

Photolysis will not contribute to the dissipation of clopyralid in soil according the available study.

Dissipation of clopyralid under field conditions was investigated in two field dissipation studies in five different sites located in the United Kingdom, Denmark, France (2 Northern sites) and Germany. Clopyralid was applied as formulated LONTREL (EF-1136) however no degradation products or bounded residue were analyzed in these field trials.

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

Degradation rate of clopyralid under aerobic and anaerobic conditions was investigated in the same studies used to establish the route of degradation in soil.

At an application rate of 0.3 mg / kg (corresponding to 225 g a.s. / ha) and 40 % MWHC clopyralid is moderate to medium persistent ($DT_{50\ 20ºC}$ = 13 d – 65 d). Degradation seems to be slower when higher application rates are used (1.0 mg / kg: $DT_{50\ 20ºC}$ = 57 d – 215 d).

Under anaerobic conditions there is practically no degradation and half life is estimated to be greater than one year.

In the field studies clopyralid dissipated slightly faster being low to moderate persistent ($DT_{50\ field}$ = 2 – 24 d). Half lives were calculated taking in to account residues found in the 0-10 cm and 10-20 cm soil layers. Residues were not measured at deeper horizons.

PECs soil were calculated based on the maximum seasonal rate without degradation between applications. Only initial PEC in soil is used in the ecotoxicological risk assessment.

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

Three batch soil adsorption/desorption studies are available for clopyralid. In these studies adsorption / desorption has been tested in four German soils and four soils from USA. The results of these studies indicate that clopyralid is very high mobile (Koc = 0.4 – 12.9 mL / g).

Four lysimeter studies are available that show exceedance of 0.1 µg / L at individual data points but not as annual average. However, none of these lysimeter studies represent the worst case GAP since the use rates are slightly lower than the typical single application rates. All lysimeter studies available have been conducted with a single application and the risk following multiple applications or after uses in consecutive years is not covered by these studies. For the first of the studies only interim report after two years was available in the original dossier. Final report was made available to the RMS during the Peer Review and assessed in the Addendum 1 (December 2004). This Addendum was discussed in the experts' meeting. Results after third year for two of the four lysimeters confirm the results obtained during the first two years.

An ongoing lysimeter study using clopyralid (Lontrel 100) following autumn application to oilseed was being performed and required by the RMS. However, notifier has indicated to the RMS their wish not to support anymore autumn uses and these uses are labelled grey in the table of representative uses. Neither interim nor final reports of the lysimeter study after the autumn application (Study K84) have been submitted. MS may need to require it for their assessment.

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

In sterile buffer solutions at 50 °C clopyralid was found to be stable for five days to hydrolysis at environmental relevant pH 4 to 9. Therefore, clopyralid is expected to be stable to hydrolysis for more than 30 d at 20 °C.

The photochemical degradation of clopyralid in water was investigated in sterile aqueous buffer solutions at pH 7 under natural sunlight at 25 °C. Minimal degradation was observed indicating that photodegradation will not be an environmental significant degradation pathway for clopyralid.

A ready biodegradability test indicated that clopyralid should be classified as a non ready biodegradable substance. However, the RMS informed the meeting that has proposed to ECB not to classify with R53 based on the ecotoxicological assessment.

A study with two water sediment systems is available. Clopyralid partitions slowly from the water to the sediment ($DT_{50\ water}$ = 128 d – 167 d) and reaches a maximum of 30.6 % AR after 100 d into the sediment. There is practically no degradation of clopyralid in the water sediment system and up to 91 % AR remains as clopyralid at the end of the experiment after 100 d (extrapolated $DT_{50\ whole\ system}$ > 500 d). Non extractable radioactivity in the sediment amounted at the end of the study (100 d) to 5.85 % AR. The amount of CO_2 formed slowly increased to 2.3 % and 5.3 % AR after 100 d.

PEC sw were calculated based on the critical GAP from the table of representative uses and spray drift loadings. FOCUS sw was not used but run off and drainage were considered in the DAR. For run off PEC sw were calculated based on a 0.5 % run off from a 1 ha field to a 0.2 ha surface and 1m depth pond. For contamination through drain flow UK scheme was followed,[3] giving higher concentrations than those obtained by spray drift. This value was used for the risk assessment presented in the DAR. As for PEC sw, also drain flow PEC sed was the highest one. Therefore, EFSA proposes that a comprehensive aquatic risk assessment taking into account spray drift, run-off, drainage and the effectiveness of potential risk mitigation measures should be conducted following the FOCUS sw scheme to confirm the results of this assessment.

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[3] PSD Data requirements handbook, Chapter 6.5, pp 32-35. PSD, Mallard House, Kings Pool, 3 Peasholme Green, York, YO107OX.
http://www.pesticides.gov.uk/psd_pdfs/registration_guides/data_reqs_handbook/env_fate.pdf

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

PEC gw of clopyralid were estimated using FOCUS-PELMO 2.2.2. for the applicable EU scenarios and the representative uses. Input parameters were selected according FOCUS guidelines and mean normalized (20 ºC, pF2) laboratory half life (DT_{50} = 36 d) was used. All applications were modelled to represent post-emergence consecutive annual applications for 20 years. Calculated 80th percentile of annual average concentrations of clopyralid at 1 m depth show that the 0.1 µg /L is exceeded for all the relevant scenarios corresponding to the spring application to winter oil seed rape, autumn application to winter and summer oilseed rape, spring application to spring cereals and autumn application to pasture. Also 0.1 µg /L is exceeded for two of the three relevant scenarios for spring application to summer oilseed rape, eight of the nine scenarios for spring application to sugar beet and for the spring application to winter cereals and six of the nine scenarios for spring application to pasture.

In the original dossier the notifier provided recalculations for spring application to winter oilseed rape and spring application to winter and spring cereals for Hamburg, Jokioinen and Okehampton scenarios using worst case field half life (DT_{50} = 24 d). Use of field degradation data for modelling potential clopyralid ground water contamination was discussed in the experts meeting. Some experts challenged that field data could be used for such a mobile compound. Based on the high rate of mineralization observed in soil degradation studies, based on that in lysimeter studies the maximum amount of AR in the leachate was 0.12 % and only 6 % AR radioactivity was found into soil and in the amount of substance found in the 10-20 cm layer in field studies, experts meeting accepted the use of field studies degradation half lives for modelling ground water. However, the experts meeting considered that all scenarios should be modelled and that, in agreement with FOCUS recommendations mean DT_{50} could be used instead of worst case. Therefore, new modelling was required. Notifier has recently submitted to the RMS a letter containing results of a new calculation following experts meeting requirement. These calculations have been summarized by the RMS in addendum 2 (August 2005) that has not been peer reviewed. Using the worst case field half life the 0.1 µg /L trigger is exceeded only for one scenario in the spring applications to sugarbeet and winter oilseed rape and cereal. When mean field half life (DT_{50} = 11 d) is used the trigger is not exceeded for any of the modelled uses and scenarios. However, according the RMS these results have been presented in a letter instead of a report; a proper report including input and output raw FOCUS files should be required to confirm these results.

Based on the peer reviewed data, MS may need to consider risk for potential ground water contamination under vulnerable situations. Autumn uses are not longer supported by the notifier and are not covered by this assessment.

4.3. FATE AND BEHAVIOUR IN AIR

Concentration of clopyralid in the air compartment and transport through it is not expected to be significant. Although photochemical oxidation in atmosphere is slow (DT_{50} = 19.5 d) has a low vapour pressure and its Henry's law constant indicates that its partitioning into air is negligible. According one available study, evaporation of clopyralid from soil and plant surfaces is minimal.

5. Ecotoxicology

Clopyralid was discussed at the EPCO experts' meeting for ecotoxicology (EPCO 17) in January - February 2005.

5.1. Risk to terrestrial vertebrates

Plant protection products containing clopyralid are to be applied to arable crops and pasture in spring, therefore birds and mammals feeding on cereal shoots, foliage, earthworms and/or insects may be at risk of exposure. The risk to birds and mammals was calculated according to the Guidance Document on Birds and Mammals (SANCO/4145/2000). Maximum application rates according to the proposed GAP as a single application was used.

To assess the risk to birds a large grazing herbivorous bird, a small insectivorous bird and a medium sized bird feeding on earthworms were considered. All calculated TER values for the relevant standard scenarios are well above the Annex VI trigger for acute, short-term and long-term exposure. The risk to birds is therefore considered as low.

To assess the risk to mammals a 10 g insectivorous mammal and a 25 g herbivorous mammal was considered. All calculated TER values for the relevant standard scenarios are above the Annex VI trigger for acute and short-term exposure. The RMS did not consider a specific long-term risk of clopyralid as necessary, since there will be no opportunity for terrestrial vertebrates to feed exclusively on contaminated diet for long periods after clopyralid application. The residue levels in pasture were in average 3.9 mg/kg one week after an application of 200-240 g as/ha. The TER_{lt} calculated based on this concentration would be at a minimum of 20, based on the NOAEL of 110 mg as/kg bw/day from the rabbit reproduction study. Even without taking into consideration any further dissipation of residues after 1 week, this TER exceeds the Annex VI trigger of 5 for long-term risk. The first tier long-term TER for a small herbivorous mammal in grassland (worst case), calculated according to the guidance document has a value of 8. Therefore the long-term risk is considered as low.

No studies on toxicity of the formulation to birds and mammals are available. The formulation has been shown to be not more toxic than the parent clopyralid to other organism groups and therefore the RMS considered the risk assessment on active ingredient to cover also the risk from the formulation.

Clopyralid would be expected to have negligible potential to bioaccumulate in animal tissues, as indicated by a log K_{ow} value of -2.63 at pH 7 and a fish BCF of <1. Consequently, the risk of secondary poisoning for mammals arising from clopyralid applications is also considered to be negligible.

5.2. RISK TO AQUATIC ORGANISMS

Based on the results from studies available with fish, *Daphnia* and algae the acute toxicity of clopyralid is considered as low. During the experts meeting one Member State informed about a green algae study submitted for national registration with a lower value for the toxicity endpoint. The meeting agreed on a data requirement for the applicant to submit this study and for the RMS to give a statement on the validity of the study and to summarise it in an addendum, if considered valid. The study is not available for the applicant. Instead another study on green algae was submitted and summarised in addendum 2 (04.07.2005). This study was not considered valid by the RMS. Furthermore, the validity of the study on the blue-green algae *Anabena flos-aqua* was questioned by one Member State at the experts' meeting. A data requirement was set for the applicant to submit primary data for the study or to submit a new study. Additional data from the study is presented in addendum 2 (04.07.2005). The RMS considers the study to be of acceptable quality and no further testing required. A low toxicity to blue-green algae is indicated, and since the TER value for algae is well above the Annex VI trigger (TER = 1370) the risk is considered low and no further studies are required.

Chronic toxicity data is available for fish (ELS-study on *Pimephales promelas*), *Daphnia* and *Chironomus riparius* water spiked test).

The risk from exposure of surface water via spray drift, run-off and drain flow was assessed separately. The predicted environmental concentration in surface water due to spray drift was calculated based on 2.77% drift to a 30 cm static water body at 1 m distance based on a single applications of 0.3, 0.15 and 0.24 kg a.s./ha for oilseed rape & sugar beet, cereals and pasture respectively. To estimate the risk from drain flow the PEC_{SW} was calculated using the UK drain flow scenario. A maximum total application rate of 300 g/ha gave a PEC of 21.9 µg/L. This value was also used to calculate the PEC_{SED} following drain flow. All first tier TER values were calculated based on initial concentrations via drain flow route of exposure, which gave the highest PECsw. For all aquatic organism assessed, the acute and long-term TER values are well above the Annex VI trigger indicating a low risk. The lowest TER value is 320 for long-term risk to invertebrates at an application rate of 0.3 kg a.s./ha.

A separate risk assessment based on the predicted run-off from treated fields was not conducted. A theoretical run-off PEC_{SW} was calculated assuming 0.5% run-off from a 1 ha field into a 1 m deep pond of 0.2 ha. In all cases, no crop intercept was assumed. This gave theoretical initial run-off PEC_{SW} values of 0.375 µg/L for oilseed rape, sugar beet and cereals uses, and 0.3 µg/L for pasture use. Since these concentrations are only 27% of those arising from spray drift, a separate risk assessment for run-off is considered to be unnecessary.

There were no major metabolites (>10% of applied radioactivity) of clopyralid detected in the water/sediment studies.

All acute and long-term TER values are well above the relevant Annex IV trigger and therefore the risk to aquatic organisms is considered low.

5.3. Risk to bees

The available studies with clopyralid and the formulated product indicate a low oral and contact toxicity to honeybees and the calculated HQ values are well below the Annex VI trigger indicating a low risk.

5.4. Risk to other arthropod species

Laboratory studies on toxicity are available for the two standard species *Aphidius rhopalosiphi* and *Typhlodromus pyri* with a formulated product that the RMS considered comparable to the lead formulation. Additional laboratory studies are available with the foliar dwelling *Crysoperla carnea,* the ground dwelling species *Poecilus cupreus* and *Pardosa* spp. and the soil dwelling species *Aleochara bilineata*.

Some sublethal effects were seen on the parasitic wasp *Aphidius rhopalosiphi* and *Typhlodromus pyri*, but no effect on mortality was observed. All other species tested exhibited no lethal or sub-lethal effects when exposed to the highest rate tested of 200 g clopyralid/ha. From this the RMS concluded that the LR_{50} values for clopyralid to *A. rhopalosiphi* and *T. pyri* would be clearly in excess of 200 g a.s./ha. This value was therefore used to perform a tier 1 risk assessment and to calculate a Hazard Quotient (HQ) as defined by ESCORT 2. The derived in-field HQ value is 1.5 for the highest application rate of 0.3 mg a.s./ha for sugar beet and oilseed rape and therefore the risk to non-target arthropods was considered low.

5.5. Risk to earthworms

Studies on the acute toxicity to earthworms from clopyralid and the formulated product indicate a low toxicity. Additionally, a long-term study with the formulation is available at an application rate of 1500 g a.s./ha. Both acute and long-term TER values are above the AnnexVI trigger and therefore the risk to earthworms is considered to be low.

No major soil metabolites of clopyralid were detected in the soil degradation studies.

5.6. Risk to other soil non-target organisms

No data on other soil non-target macro-organisms are available since DT_{90} <365 days and no adverse effects were observed in the tests with earthworms, ground or soil dwelling arthropods, or soil micro-organisms.

5.7. Risk to soil non-target micro-organisms

The effects of clopyralid on soil carbon and nitrogen conversion were tested. No deviations of more than 25% after 28 days were observed. Hence the Annex VI trigger was met indicating a low risk.

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

Vegetative vigour was assessed for *Avena sativa*, *Allium cepa*, *Cyperus esculentus*, *Brassica napus*, *Beta vulgaris and Glycine max* with the formulation Lontrel 100. The ER_{50} for the most sensitive species *Glycine max* is 25.4 g a.s./ha. In the DAR, PEC values were calculated based on a spray drift of 2.77% at 1 m distance and a maximum application rate of 120 g a.s./ha in a single application. The TER value calculated from these assumptions is 7.7, hence indicating a low risk to non-target plants outside the treated field. The application rate was however discussed in the experts' meeting since maximum application according to the GAP is 240 g a.s./ha. Based on this higher application rate the resulting TER values are 3.8 and 18.5 respectively, at 1 and 5 m distance from the treated field. This indicates that at 240 g a.s./ha as proposed for pasture, buffer zones of 5 m or other drift reducing measures are necessary to protect non-target plants outside the field. Also for the second application of 200 g a.s./ha as proposed for oilseed rape and sugar beet in some parts of Europe the same risk mitigation has to be applied.

5.9. Risk to biological methods of sewage treatment

Data from a test with activated sludge are available and indicate that the risk to biological methods of sewage treatment plants is low.

6. Residue definitions

Soil

Definitions for risk assessment: clopyralid and its salts

Definitions for monitoring: clopyralid and its salts

Water

Ground water

Definitions for exposure assessment: clopyralid and its salts

Definitions for monitoring: clopyralid and its salts

Surface water

Definitions for risk assessment: clopyralid and its salts

Definitions for monitoring: clopyralid and its salts

Air

Definitions for risk assessment: clopyralid and its salts

Definitions for monitoring: clopyralid and its salts

Food of plant origin

Definitions for risk assessment: clopyralid, its salts and conjugates, expressed as clopyralid

Definitions for monitoring: clopyralid, its salts and conjugates, expressed as clopyralid

Note: Subject to availability of a validated enforcement method a residue definition of clopyralid (including salts) might be a valid alternative. (refer to 3.1.1)

Food of animal origin

Definitions for risk assessment: clopyralid, its salts and conjugates, expressed as clopyralid

Note: proposed after the experts' meeting by EFSA, agreed to by RMS, not peer reviewed

Definitions for monitoring: clopyralid, its salts and conjugates, expressed as clopyralid

Note: proposed after the experts' meeting by EFSA, agreed to by RMS, not peer reviewed

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Clopyralid	Moderate persistent (DT_{50lab} (20 ºC) = 13 – 65 d)	Acute and long-term risks to terrestrial organisms are acceptable (assessed in the DAR).

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth FOCUS for the representative uses	Pesticidal activity	Toxicological activity	Ecotoxicological activity
Clopyralid	Very Highly mobile	FOCUS modelling: Yes Lysimeter study: No	Yes	Yes, assessed in the DAR.	Yes, assessed in the DAR.

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Clopyralid (water and sediment phases)	Acute and long-term risks to aquatic and sediment organisms are acceptable (assessed in the DAR).

Air

Compound (name and/or code)	**Toxicology**
Clopyralid	Air contamination not expected.

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

- A validated analytical method for the determination of residues in food of animal origin (incl. an ILV) (relevant for all representative uses; submission date unknown; data gap identified by EFSA after the expert meetings, refer to chapter 1).
- Processing studies are required (relevant for the use on cereals, not yet submitted, refer to point 3.1.1).
- Further data on crop rotation may be required (relevant for uses on cereals, sugar beet, and oilseed rape; submission date unknown, data gap identified by EFSA after the experts' meetings, refer to point 3.1.2).
- The following experimental reports are required in order to assess the validity of the respective metabolism and feeding studies:

  - N.N., Experimental report on metabolism study in goats, Analytical Development Corporation, 1983. (relevant for all uses, submission date unknown, data gap identified by EFSA after the experts' meetings; refer to point 3. 2)

  - Templeton, J.A., DOW Report GH-A579, March 12, 1974 (relevant for all uses; submitted to RMS 8 Sep 2005; refer to point 3. 2)

  - Swart, R.W. and Boswell, C.R., DOWCO 290 and 2,4 D chicken feeding study. Report TA 517, 1974 (relevant for all uses; submitted to RMS 8 Sep 2005; refer to point 3. 2).
- Risk assessment presented in the DAR follow the UK-PSD scheme to assess potential surface water contamination by drainage, showing that this route may be more important than spray drift. Therefore, EFSA proposes that a comprehensive aquatic risk assessment taking into account spray drift, run-off, drainage and the effectiveness of potential risk mitigation measures should be conducted following the FOCUS sw scheme to confirm the results of this assessment (refer to point 4.2.1).
- MS may need to require final report of the lysimeter study after the autumn application (Study K84) for their assessment (relevant for autumn uses; no submission date proposed by the notifier; refer to point 4.2.2).
- New FOCUS gw modelling for all representative uses and scenarios as required by experts meeting (EPCO 16). Results of this modelling have been presented by the notifier to the RMS in a letter. This new information has been summarized by the RMS in addendum 2 (August 2005) and has not been peer reviewed. However, a report including input and output raw FOCUS gw files of this new modelling exercise should be required to confirm the results (relevant for all uses; summary results presented as a letter to the RMS, no submission date proposed by the notifier for the full report; refer to point 4.2.2).
- A data requirement was set for the applicant to submit primary data for the study on blue-green algae or to submit a new study. These data were summarized by the RMS in addendum 2 (August 2005) and considered acceptable but have not been peer reviewed; (refer to point 5.2).

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 comprises broadcast spraying to control a narrow spectrum of broad-leaved weeds in cereals, oilseed rape, sugar beet and pasture at application rate up 127 g clopyralid per hectare for cereals, up to 300 g for oilseed rape and sugar beet, and up to240 g for pasture. Clopyralid can be used only as herbicide.

The representative formulated product for the evaluation was "Lontrel 100", a soluble concentrate (SL), registered under different trade names in Europe.

Adequate methods are available to monitor all compounds given in the respective residue definition, except for food of animal origin.

Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.

Sufficient analytical method 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.

Clopyralid is rapidly and nearly completed absorbed in the rat. It is widely distributed and the highest concentration was found in the liver. There was no evidence of accumulation. Clopyralid is not metabolised. The acute toxicity is low i.e. oral LD_{50} > 5000 mg/kg bw, dermal LD_{50} > 2000 mg/kg bw and inhalatory exposure LC_{50} > 1 mg/L air. It does not induce skin irritancy or sensitization. However, clopyralid induced a marked irritation in the eyes of the rabbit and the symptoms persisted after 21 days. Thus, the proposed **classification for acute toxicity is Xi; R41"Risk of serious damage to eyes"**

It is not genotoxic, carcinogenic or toxic towards reproduction.

The ADI and AOEL is 0.15 and 0.1 mg/kg bw/day, with a safety factor of 100 applied. No ARfD is set.

A default of 10% for dermal absorption is set for Lontrel 100. The estimated operator exposure is below the AOEL even without PPE (34%), according to the UK POEM model.

No extensive metabolism occurred in the crops studied and hence clopyralid was found to be the major component of the residue in plants. The metabolism of clopyralid was similar in all studied crop groups and an adequate number of residue trials on the representative crops cereals, sugar beet, rape seed and pasture is available. For the use on cereals the experts' meeting for residues concluded that processing studies need to be submitted.

Significant amounts of clopyralid residues were found in potential feeding stuff. Therefore animal metabolism was investigated in ruminants and in poultry, indicating the majority of the residue found in animal matrices being clopyralid in free and conjugated form (the latter mainly in milk). From the study it was concluded that, apart from conjugation with glycin, clopyralid was not metabolised in livestock and that the occurrence of significant residues (>0.01 mg/kg) in edible animal tissues may be expected. Thus, feeding studies with clopyralid in ruminants, hens and pigs have been evaluated. It is noted that further data need to be submitted to assess the validity of some of the metabolism and feeding studies and to confirm the proposed MRLs for food of animal origin.

Data to support the assumption that no significant residues will occur in rotational crops have not been submitted, but may be required since there are indications that clopyralid residues in soil may be taken up and accumulated in rotational crops.

In a consumer risk assessment it was demonstrated that exposure to residues resulting from the representative uses of clopyralid is well below the ADI for the considered consumer groups. Even though intake of clopyralid residues is not likely to pose a high risk to consumers the current assessment needs to be confirmed by the data still to be submitted. An acute risk for consumers through clopyralid residues on food is not anticipated, as no ARfD has been proposed.

Under aerobic conditions in soil, no degradation products of clopyralid that accounted for more than 10 % AR were identified. Non extractable radioactivity increased to a maximum of 35 % AR after 92 d. Volatiles collected in a trap with alkaline solution (attributed to CO_2) amounted up to a maximum of 83.3 % AR. Minimal degradation occurred under anaerobic conditions.

Photolysis will not contribute to the dissipation of clopyralid in soil. At an application rate of 0.3 mg / kg (corresponding to 225 g a.s. / ha) and 40 % MWHC clopyralid is moderate to medium persistent ($DT_{50\ 20°C}$ = 13 d – 65 d). Degradation seems to be slower when higher application rates are used (1.0 mg / kg: $DT_{50\ 20°C}$ = 57 d – 215 d).

In the field studies clopyralid dissipated slightly faster being low to moderate persistent ($DT_{50\ field}$ = 2 – 24 d). PECs soil were calculated based on the maximum seasonal rate without degradation between applications. Only initial PECs soil are used in the ecotoxicological risk assessment.

The batch soil adsorption/desorption studies indicate that clopyralid is very high mobile in soil (Koc = 0.4 – 12.9 mL / g).

Four lysimeter studies are available that show exceedance of 0.1 µg / L at individual data points but not as annual average. However, none of these lysimeter studies represent the worst case GAP since the use rates are slightly lower than the typical single application rates and multiple applications have not been performed. An ongoing lysimeter study using clopyralid (Lontrel 100) following autumn application to oilseed was being performed and required by the RMS. However, notifier has indicated to the RMS their wish not to support anymore autumn uses and these uses are labelled grey in the table of representative uses. Therefore, neither interim nor final reports of the lysimeter study after the autumn application (Study K84) has not been submitted. MS may need to require it for their assessment.

Clopyralid is expected to be stable to hydrolysis for more than 30 d at 20 °C at environmental relevant pH 4 to 9. Photodegradation will not be an environmental significant degradation pathway for clopyralid.

Clopyralid should be classified as a non ready biodegradable substance.

Clopyralid partitions slowly from the water to the sediment ($DT_{50\ water}$ = 128 d – 167 d) and reaches a maximum of 30.6 % AR after 100 d into the sediment. There is practically no degradation of clopyralid in the water / sediment system and up to 91 % AR remains as clopyralid after 100 d at the end of the experiment (extrapolated $DT_{50\ \text{whole system}}$ > 500 d). Non extractable radioactivity in the sediment amounted at the end of the study (100 d) to 5.85 % AR. The amount of CO_2 formed slowly increased to between 2.3 % and 5.3 % AR after 100 d.

PEC sw were calculated based on the critical GAP from the table of representative uses and spray drift loadings. FOCUS sw was not used but run off and drainage were considered in the DAR. For run off PEC sw were calculated based on a 0.5 % run off from a 1 ha field to a 0.2 ha surface and 1m depth pond. For contamination through drain flow UK scheme was followed, giving rise to higher concentrations than those obtained by spray drift. This value was used for the risk assessment presented in the DAR. As for PEC sw, also drain flow PEC sed was the higher one. Therefore, EFSA proposes that a comprehensive aquatic risk assessment taking into account spray drift, run-off, drainage and the effectiveness of potential risk mitigation measures should be conducted following the FOCUS sw scheme to confirm the results of this assessment.

PEC gw of clopyralid were estimated using FOCUS-PELMO 2.2.2. for the applicable EU scenarios using mean normalized (20 ºC, pF2) half life (DT_{50} = 36 d). Calculated 80^{th} percentile of annual average concentrations of clopyralid at 1 m depth show that the 0.1 µg /L is exceeded for all the relevant scenarios corresponding to the spring application to winter oil seed rape, autumn application to winter and summer oilseed rape, spring application to spring cereals and autumn application to pasture. Also 0.1 µg /L is exceeded for two of the three relevant scenarios for spring application to summer oilseed rape, eight of the nine scenarios for spring application to sugar beet and for the spring application to winter cereals and six of the nine scenarios for spring application to pasture.

An assessment based on field degradation data has been presented with a letter to the RMS and summarized in addendum 2 (August 2005) but has not been peer reviewed. A complete report on this new modelling is required.

Based on the peer reviewed data MS may need to consider risk for potential ground water contamination under vulnerable situations. Autumn uses are not longer supported by the notifier and are not covered by this assessment.

Concentration of clopyralid in the air compartment and transport through it is not expected to be significant.

The risk to terrestrial vertebrates, aquatic organisms, bees, non-target arthropods, earthworms and soil macro- and microorganisms from clopyralid used according to the proposed GAP is considered low based on available studies and information. For the maximum application rate proposed in a single application, 240 g a.s./ha for pasture, a 5 m buffer zone or drift reducing measures are necessary to protect non-target plants outside the field. Calculated TER values are 3.8 and 18.5 at 1 and 5 m distance respectively based on a spray drift of 2.77 %.

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

- Autumn uses are not longer supported by the notifier and are not covered by this assessment (refer to point 4.2.). High risk for ground water contamination by autumn uses is envisaged. A lysimeter study under autumn conditions is available to the applicant and may be required by MS.

- For the maximum application rate proposed in a single application, 240 g a.s./ha for pasture, a 5 m buffer zone or drift reducing measures are necessary to protect non-target plants outside the field. Calculated TER values are 3.8 and 18.5 at 1 and 5 m distance respectively based on a spray drift of 2.77 %. Also for the second application of 200 g a.s./ha as proposed for oilseed rape and sugar beet in some parts of Europe the same risk mitigation has to be applied (refer to point 5.8).

Critical areas of concern

- Clopyralid induced a marked irritation in the eyes of the rabbit and the symptoms persisted after 21 days and the proposed classification for acute toxicity proposed Xi; R41"Risk of serious damage to eyes".
- MS need to consider risk for potential ground water contamination under vulnerable situations.
- The risk to non-target plants outside the field has to be mitigated, e.g. with buffer zones of 5 m or drift reducing measures at application rates above 180 g a.s./ha.

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

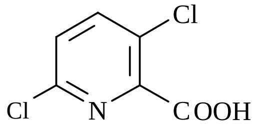
(Abbreviations used in this list are explained in appendix 2)

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

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

Rapporteur Member State	Finland
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	3,6-dichloropyridine-2-carboxylic acid
Chemical name (CA) ‡	3,6-dichloro-2-pyridinecarboxylic acid
CIPAC No ‡	455
CAS No ‡	1702-17-6
EEC No (EINECS or ELINCS) ‡	216-935-4
FAO Specification ‡ (including year of publication)	There is no FAO specification.
Minimum purity of the active substance as manufactured ‡ (g/kg)	950 g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	There are no relevant impurities.
Molecular formula ‡	$C_6H_3Cl_2NO_2$
Molecular mass ‡	191.96
Structural formula ‡	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	149.6 °C (998 g/kg)
Boiling point (state purity) ‡	Not measurable, decomposes
Temperature of decomposition	164 °C (998 g/kg)
Appearance (state purity) ‡	White, crystalline solid (998 g/kg)

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

Relative density (state purity) ‡	1.763 g/cm^3 at 20.7 ^{o}C (density) (998 g/kg)
Surface tension	55 mN/m at 21.5 ^{o}C (0.7685 % aqueous solution)
Vapour pressure (in Pa, state temperature) ‡	1.36 x 10^{-3} Pa at 25 °C (extrapolated from 36 – 65 ^{o}C) (996 g/kg)
Henry's law constant (Pa m3 mol -1) ‡	Unbuffered 3.3 x 10-10 Pa m3 mol-1 at 20 ^{o}C pH 5 2.2 x 10-11 Pa m3 mol-1 at 20 ^{o}C pH 7 1.8 x 10-11 Pa m3 mol-1 at 20 ^{o}C pH 9 1.6 x 10-11 Pa m3 mol-1 at 20 ^{o}C
Solubility in water ‡ (g/L or mg/L, state temperature)	Unbuffered: 7.85 g/L at 20 ^{o}C H
	pH 5: 118 g/L at 20 ^{o}C
	pH 7: 143 g/L at 20 ^{o}C
	pH 9: 157 g/L at 20 ^{o}C (all 992 g/kg)
Solubility in organic solvents ‡ (in g/L or mg/L, state temperature)	<u>964 g/kg:</u> acetonitrile: 12.1 wt% at 20 ^{o}C n-hexane: 0.6 wt% at 20 ^{o}C methanol: 10.4 wt% at 20 ^{o}C <u>959 g/kg:</u> acetone: >250 g/L at 20 ^{o}C, ethyl acetate: 102 g/L at 20 ^{o}C, xylene: 4.6 g/L at 20 ^{o}C 1,2-dichlorethane: 20.7 g/L at 20 ^{o}C
Partition co-efficient (log POW) ‡ (state pH and temperature)	pH 5: - 1.81 at 20 ^{o}C pH 7: - 2.63 at 20 ^{o}C pH 9: - 2.55 at 20 ^{o}C (all 992 g/kg) log P_{ow} = -2.53 Estimation by the Leo-Hansch method
Hydrolytic stability (DT50) ‡ (state pH and temperature)	pH 4-9: No hydrolysis.
Dissociation constant ‡	2.01 at 25 ^{o}C (996 g/kg)
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	Absorption maxima (nm) and ε (l/mol cm) are Unbuffered at 193, 220, 280: 22100, 9200, 4790 pH <2 at 202, 225, 281: 16200, 8890, 3800 pH >10 at 220, 279: 9300, 5030
Photostability (DT50) ‡ (aqueous, sunlight, state pH)	DT_{50}: 261 days in sterile aqueous pH 7 buffer solution at a concentration of 2.0 ppm clopyralid under natural sunlight at 25°C.
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	Not necessary to determine since clopyralid was essentially stable in the aqueous photolysis study.
Flammability ‡	Not flammable
Explosive properties ‡	Not explosive

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

List of representative uses evaluated*

Crop and/ or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
(a)			(b)	(c)	Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max	(l)	(m)
Cereals	N-EU	Lontrel 100	F	Broad leaved weeds	SL	100	B	BBCH 20-39 (Mar – Apr)	1	N/A	0.018 – 0.127	100 – 400	0.070 – 0.127	None	B: Broadcast No PHI required to restrict residue levels. [1]
Cereals	S-EU	Lontrel 100	F	Broad leaved weeds	SL	100	B	BBCH 20-45 (Feb – Apr)	1	N/A	0.018 – 0.127	100 – 400	0.070 – 0.127	None	
Pasture	N-EU	Mixtures	F	Broad leaved weeds	SL	100	B	Established pastures (Mar to Aug)	1	N/A	0.016 – 0.120	100 – 500	0.080 – 0.120	7	Pasture products only as mixtures. [1]
Pasture	S-EU	Mixtures	F	Broad leaved weeds	SL	100	B	Established pastures (Mar to Aug)	1	N/A	0.024 – 0.240	100 – 500	0.120 – 0.240	7	[1]
Oilseed rape	UK /Ireland	Dow Shield	F	Broad leaved weeds	SL	100	B	BBCH 12 (Jan-April)	2	21 days	0.040 – 0.050 + 0.080 – 0.100	200 – 250	0.100 + 0.200	None	[1]

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

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation Type (d-f)	Formulation Conc. of as (i)	Application method kind (f-h)	Application growth stage & season (j)	Application number min max (k)	Application interval between applications (min)	Application rate per treatment kg as/hl min max	Application rate per treatment water l/ha min max	Application rate per treatment kg as/ha min max	PHI (days) (l)	Remarks (m)
Oilseed rape	Rest of N-EU	Lontrel 100	F	Broad leaved weeds	SL	100	B	BBCH 12 – 32 (Feb – May)	1	N/A	0.020 – 0.150	100 – 500	0.100 - 0.150	None	
Oilseed rape	S-EU	Lontrel 100	F	Broad leaved weeds	SL	100	B	BBCH 10-51 (Mar–May)	1	N/A	0.020 – 0.150	100 – 600	0.120 - 0.150	None	
Sugar beet	UK/ Ireland	Lontrel 100	F	CIRAR	SL	100	B	BBCH 10 (Mar – Jun)	2	21 days	0.050 – 0.125 + 0.100 – 0.250	80 - 200	0.100 + 0.200	None	
Sugar beet	Rest of N-EU	Lontrel 100	F	CIRAR	SL	100	B	BBCH 10-39 (Apr – Jul)	2	21 days	0.050 – 0.125 + 0.100 – 0.250	80 - 200	0.100 + 0.200	None	
Sugar beet	S-EU	Lontrel 100	F	CIRAR	SL	100	B	BBCH 14-19 (Apr-Jun)	1	N/A	0.075 – 0.188	80 - 200	0.150	None	

[1] The risk assessment has revealed data gaps in section 4.

Remarks:	*	Uses for which risk assessment could not been concluded due to lack of essential data are marked grey	(h)	Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
	(a)	For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)	(i)	g/kg or g/L
			(j)	Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants,

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

	(b)	Outdoor or field use (F), glasshouse application (G) or indoor application (I)		1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
	(c)	*e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds		
	(d)	*e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)	(k)	The minimum and maximum number of application possible under practical conditions of use must be provided
	(e)	GCPF Codes - GIFAP Technical Monograph No 2, 1989		
	(f)	Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench	(l)	PHI - minimum pre-harvest interval
	(g)	All abbreviations used must be explained	(m)	Remarks may include: Extent of use/economic importance/restrictions

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

Appendix 1.2: Methods of Analysis

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

Technical as (principle of method)	GC-FID, silica capillary column
Impurities in technical as (principle of method)	GC-FID, silica capillary column
Plant protection product (principle of method)	HPLC, UV-detection at 275 nm, RP-18 column

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	GC-MSD, 0.01 mg/kg (cereals, sugar beet) GC/NCI-MS, 0.01 mg/kg (rape seed)
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	GC/MSD, 0.01 mg/kg (for all products) *The validation extent is not in accordance with SANCO/825/00 and an ILV is missing.*
Soil (principle of method and LOQ)	GC/ MSD, 0.5 µg /kg
Water (principle of method and LOQ)	GC/MSD, 0.05 µg/L for surface, ground and drinking water
Air (principle of method and LOQ)	GC/MSD, 15 µg/m^3
Body fluids and tissues (principle of method and LOQ)	Not relevant, clopyralid is not toxic or very toxic

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	None

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

Appendix 1.3: Impact on Human and Animal Health

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

Rate and extent of absorption ‡	Rapidly and completely absorbed
Distribution ‡	Extensive, low tissue levels (<0.01% of applied dose)
Potential for accumulation ‡	No evidence of accumulation
Rate and extent of excretion ‡	Rapidly excreted unchanged via urine (>80% in 24 h)
Metabolism in animals ‡	None
Toxicologically significant compounds ‡ (animals, plants and environment)	Clopyralid

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 5000 mg/kg bw
Rat LD_{50} dermal ‡	> 2000 mg/kg bw (rabbit)
Rat LC_{50} inhalation ‡	> 1 mg/L (highest attainable concentration)
Skin irritation ‡	Mildly irritating, no classification proposed
Eye irritation ‡	Severely irritating to eyes **R41**
Skin sensitization ‡ (test method used and result)	Slightly sensitising, no classification proposed

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Haematological effects and increase in liver weight
Lowest relevant oral NOAEL / NOEL ‡	100 mg/kg bw/day in dogs
Lowest relevant dermal NOAEL / NOEL ‡	>1000 mg/kg bw/day
Lowest relevant inhalation NOAEL / NOEL ‡	No data, not required

Genotoxicity ‡ (Annex IIA, point 5.4)

No genotoxic potential

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

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

Target/critical effect ‡	Lesions of the gastric limiting ridge in rats
Lowest relevant NOAEL / NOEL ‡	15 mg/kg bw/day in rats
Carcinogenicity ‡	No carcinogenic potential

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Decreased pup weights and increased pup liver weights in F1 generation at maternally toxic dose levels.
Lowest relevant reproductive NOAEL / NOEL ‡	Parental toxicity: 150 mg/kg bw/day Offspring toxicity: 500 mg/kg bw/day Reproductive toxicity: >1500 mg/kg bw/day
Developmental target / critical effect ‡	Decreased mean foetal weight and slightly increased spontaneous malformations in rabbits at maternally toxic dose levels.
Lowest relevant developmental NOAEL / NOEL ‡	Rat maternal: 75 mg/kg bw/day and developmental > 250 mg/kg bw/day. Rabbit maternal and developmental: 110 mg/kg bw/day.

Neurotoxicity / Delayed neurotoxicity ‡ (Annex IIA, point 5.7)

	No data, not required.

Other toxicological studies ‡ (Annex IIA, point 5.8)

	A comparison of technical material produced by two different manufacturing processes showed similar toxicity profiles.

Medical data ‡ (Annex IIA, point 5.9)

	No detrimental effects on health in manufacturing personnel and no reports in open literature about adverse health effects in humans.

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

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.15 mg/kg bw/day	Rat 2-year combined chronic toxicity and carcinogenicity study	100
AOEL ‡	1.0 mg/kg bw/day	1-year study in dog	100
ARfD ‡ (acute reference dose)	Not allocated, not relevant		

Dermal absorption (Annex IIIA, point 7.3)

	No data submitted 10% as default for concentration and spray dilution.

Acceptable exposure scenarios (including method of calculation)

Operator	The estimated operator exposure according to the UK POEM model is below the AOEL. The maximum applied dose is 0.2 kg/ha using tractor mounted boom with hydraulic nozzles. Without PPE 34% With PPE 4%
Workers	The estimated worker exposure is below the AOEL, approximately < 4%.
Bystanders	The estimated acute exposure of a bystander is below the AOEL, approximately < 1%.

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	Xi Irritant R41 Risk of serious damage to eyes

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

Appendix 1.4: Residues

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

Plant groups covered	Rapeseed (P/O), sugar beet (R), cabbage (L), pasture No qualitative metabolism differences between the crops.
Rotational crops	Not investigated, data may be required
Plant residue definition for monitoring	Clopyralid, its salts and conjugates, expressed as clopyralid
Plant residue definition for risk assessment	Clopyralid, its salts and conjugates, expressed as clopyralid
Conversion factor (monitoring to risk assessment)	None

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

Animals covered	Lactating goats, laying hens
Animal residue definition for monitoring	Clopyralid, its salts and conjugates, expressed as clopyralid
Animal residue definition for risk assessment	Clopyralid, its salts and conjugates, expressed as clopyralid
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No

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

....	Data not submitted, confirmatory data may be required

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

Maize fodder, grain and forage	12 months
Pasture	18 months
Oil containing plant materials (rape seed)	18 months
Tissues (muscle, liver kidney), eggs and milk	Not evaluated by RMS, availability unknown

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

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

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: yes	Poultry: yes	Pig: yes
Muscle	0.10 mg/kg	0.05*mg/kg	0.05* mg/kg
Liver	0.10 mg/kg	0.05*mg/kg	0.05* mg/kg
Kidney	0.50 mg/kg	0.05*mg/kg	0.05* mg/kg
Fat	0.05* mg/kg	0.05*mg/kg	0.05* mg/kg
Milk	0.02 mg/kg	n/a	n/a
Eggs	n/a	0.05* mg/kg	n/a

* LOQ
n/a not applicable

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

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

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL	STMR (b)
Barley	N-EU	0.14, 0.24, 0.34, 0.37, 0.38, 0.47, 0.61, 0.82, 0.95	Based on extrapolation from wheat	2.0 mg/kg	0.60
	S-EU	0.13, 0.68, 1.16, 1.34	Based on extrapolation from wheat		0.68
Barley straw	N-EU	0.17, 0.28, 0.31, 0.40, 0.50, 0.87, 1.05, 1.08			0.42
	S-EU	0.59, 0.84, 1.16, 1.20			0.92
Wheat	N-EU	0.07, 0.23, 0.73, 0.79, 0.93, 1.06, 1.11, 1.26	Extrapolate to barley	2.0 mg/kg	0.60
	S-EU	0.26, 0.68, 1.16, 1.42	Extrapolate to barley		0.68
Wheat straw	N-EU	0.26, 0.59, 0.79, 0.93, 1.06, 1.11, 1.26			0.42
	S-EU	0.39, 0.63, 0.99, 1.18			0.93
Rapeseed	N-EU	0.03, 0.05, 0.02, 0.1, 0.04, 0.01, 0.02, 0.01	None	0.1 mg/kg	0.02
	S-EU	0.02, 0.01, 0.01, 0.01	None		0.01
Sugar beet roots	N-EU	0.36, 0.34, 0.29, 0.41, 0.35, 0.56, 0.21, 0.17, 0.12, 0.80	None	1.0 mg/kg	0.35
	S-EU	0.22, 0.42, 0.23, 0.14, 0.13, .012 , 0.06, 0.14	None		0.14

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

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL	STMR (b)
Sugar beet tops	N-EU	0.13, 0.14, 0.23, 0.36, 0.47, 0.62, 1.05			0.42
	S-EU	0.12, 0.16, 0.16, 0.17			0.16
Pasture	N-EU	2.6, 2.8, 3.0, 4.4, 5.0, 5.4	Though intended dose rate for S-EU is twice higher than for N-EU, this higher rate was used to produce the N-EU and S-EU data.		3.7
	S-EU	3.4, 3.9, 4.0, 8.5			4.0

N-EU=Northern Europe, S-EU=Southern Europe

(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 critical GAP

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

ADI	0.15 mg/kg bw/day
TMDI (European Diet) (% ADI)	6 % (WHO European diet, adult 60 kg)
NEDI (% ADI)	11 % (German diet, female child 13.5 kg)
Factors included in NEDI	Not required
ARfD	Not required
Acute exposure (% ARfD)	Not required

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Rapeseed oil	15	0.1	-
Sugar beet	>1	0.01	-

* Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies

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

Cereal grain	2.0 mg/kg
Rapeseed	0.1 mg/kg
Sugar beet	1.0 mg/kg
Ruminant kidney +	0.5 mg/kg
Ruminant meat, ruminant liver +	0.1 mg/kg
Fat, meat and offal except ruminant meat and offal +	0.05* mg/kg
Milk +	0.02 mg/kg
Eggs +	0.05* mg/kg

*) LOQ

+ Subject to validity of the underlying studies, to be confirmed; not peer reviewed

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

Appendix 1.5: Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	CO_2: 47.5 – 65.5 % of AR after 92 days, 72.9 – 83.3 % of AR after 374 days at 20 ˚C, [2,6-pyridinyl-^{14}C]-label (n=5) Sterile conditions: no studies provided nor required
Non-extractable residues after 100 days ‡	11.2 – 35.1 % of AR after 92 days at 20 ˚C, [2,6-pyridinyl-^{14}C]-label (n=5) Sterile conditions: no studies provided nor required
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	No major metabolites in addition to CO_2 Unidentified minor metabolites max. 7.7 % of AR at 20 ˚C

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

Anaerobic degradation ‡	No mineralisation, NER max 13.4 % of AR after 30 days, no metabolites at 20 ˚C, [2,6-pyridinyl-14C]-label (n=1)
Soil photolysis ‡	No photolysis: >89 % of AR unchanged clopyralid, NER max 5 % of AR , up to 3 % CO_2 after 30 days, no photoproducts were identified, DT_{50} >12 years, [2,6-pyridinyl-^{14}C]-label (n=1)

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

Method of calculation	First order kinetics: Solver function in a Microsoft Excel spreadsheet was used.
Laboratory studies (range and mean or median, with n value, with r^2 value)	DT_{50lab} (20°C, aerobic):13, 16, 28, 36, 45, 65 days, mean = 34 days, R^2 = 0.978 – 0.991 (n=6)
	DT_{90lab} (20°C, aerobic): 43, 54, 93, 120, 150, 217 days, mean = 113 days, R^2 = 0.978 – 0.991 according to DT_{50} quoted above (n=6)
	DT_{50lab} (10°C, aerobic): 73, 100, 198 days, mean = 124 days, DT_{90lab}: 224, 331, 657 days, R^2 = 0.963 – 0.969 (n=3)
	DT_{50lab} (20°C, anaerobic): >1 year (n=1)

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

	For FOCUS GW modelling: 1st tier modelling (aerobic, first order kinetics): mean DT_{50lab} = 36 days (normalised to 10kPa) higher tier modelling (field dissipation kinetics): worst case $DT_{50field}$ = 24 days or mean $DT_{50field}$ = 11 days
	degradation in the saturated zone: no degradation, mainly partitioned in aqueous phase
Field studies (state location, range and mean or median with n value)	bare soil, first order DT_{50f}: mean = 11 days (n=5) Spalding, UK: 8 days, R^2 = 0.715, n=1 Middlefart, DK: 24 days, R^2 = 0.953, n=1 Ansonville, F: 2 days, R^2 = 0.968, n=1 (autumn appl.) Mainbervilliers, F: 7 days, R^2 = 0.976, n=1 (autumn) Oederquart, D: 16 days, R^2 = 0.954, n=1 (autumn appl.) DT_{90f}: locations as above, 6, 24, 28, 54, 79 days, mean = 38 days (n=5)
Soil accumulation and plateau concentration	Clopyralid does not accumulate in soil due to its rapid mineralisation and high mobility in soil. No studies provided nor required.

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

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡	1) European soils: K_{oc} 3.43, 4.76, 5.04, 7.34, mean = 5.15, K_d = 0.032, 0.048, 0.051, 0.151, mean = 0.071 R^2 = 0.99, mean 1/n = 0.6473 (n=4) 2) American soils: K_{oc} 0.40, 2.12, 3.15, 12.90, mean =4.64, K_d = 0.0094, 0.020, 0.042, 0.0935, mean = 0.041 R^2 = 0.548 – 0.993, mean 1/n = 0.875 (n=4) For FOCUS GW modelling the mean value of the two studies were used: K_{oc} = 4.9 and 1/n = 0.761 (n=8)
pH dependence ‡ (yes / no) (if yes type of dependence)	Yes. Limited evidence that clopyralid is less mobile in acidic soil: K_{oc} was 98.64 at pH 4.06 and 4.76 at pH 5.34 in different horizons of Kaldenkirchen soil; 14.61 at pH 6.21 and 11.25 at pH 6.68 in Lanna soil (n=4).

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

Column leaching ‡	No studies with freshly applied clopyralid submitted nor required
Aged residues leaching ‡	Guideline: BBA Merkblatt 37. One soil, 40 days of ageing, 400 ml of precipitation, time not indicated: 75 % of AR recovered in column leachate as unchanged clopyralid. In the top 3 cm of the soil 6.1 % of AR. After 99 days of ageing and 400 ml of precipitation: 4 % of AR in column leachate as unchanged clopyralid. In the top 3 cm of the soil 19.6 % of AR.

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

Lysimeter/ field leaching studie ‡	Study type: lysimeter studies 1) Germany, spring application of 150 or 200 g clopyralid/ha on oilseed rape + partly a second application of 125 g a.s./ha on winter wheat 1 year later: A total of 935 mm of precipitation was received in year 1 and 895.5 mm in year 2. 438 – 478 L of leachate was collected in year 1 and 411-437 L in year 2. In the first year of application the annual average concentration in leachate was < 0.050 µg/L ai equivalent, however occasional exceedings of 0.10 µg/L were detected. In the second year the annual average concentration in leachate was < 0.055 µg/L. In the soil cores the majority of radioactivity remained in the top layers of 0 – 40 cm. 11.49 – 12.38 % of AR was found in soil 2 years after the single application. In the third year the annual average concentration in leachate was 0.001 – 0.019 µg/L. Maximum concentration of ai equivalents in leachate of the third year was 0.043 µg/L in the lysimeter which received two applications. In the soil cores 9.82 – 10.11 % of RA was found 2 years after the second application. The total recovery of RA in the three year monitoring period was 12.81 – 17.53 % of the applied RA, considering the both applications. 2) Germany, winter oilseed rape, 120 or 141 g clopyralid/ha, 847 and 1011 mm rain in years 1 and 204 – 417 mm of leachate was collected in two lysimeters in years 1 and 2. In the lysimeter with higher application rate the annual average concentration of unidentified radioactivity was 0.127 µg/L equivalent in year 1, but taken over the whole study period of two years, the average concentration was 0.064 – 0.078 µg/L equivalent. Occasional exceedings of 0.1 µg/L were detected soon after the application in both lysimeters.

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

	3) Germany, sugar beet, spring application of 118 g clopyralid/ha, 754 and 871 mm rainfall in years 1 and 2: 113 and 196 mm of leachate was collected in years 1 and 2. Annual average concentrations of clopyralid were 0.010 and 0.002 µg/L in years 1 and 2. Non-extractable radioactivity was also present in the leachate at annual average concentrations of 0.113 and 0.031 µg/L equivalent in years 1 and 2, respectively. Dissolved CO2 was the major metabolite observed in the leachate. 24.6 % of AR was measured in soil after 111 days, and after 2 years 13.2 % of AR was recovered. 4) Germany, sugar beet, spring application of 99 or 185 g clopyralid/ha, ca 700 mm rainfall/year: In year 1 the leachate volume was 180 and 248 mm, and in year 2 70 to 79 mm. Annual average concentrations in the leachate were not calculated, but in individual samples the clopyralid concentrations up to 0.135 µg/L were detected occasionally. 26 months after application 20 % of AR was recovered from the soil, majority of it in tillage layer (0 – 30 cm).

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	Maximum seasonal application rate, no degradation assumed between the applications, evenly distributed in the top 5 cm of soil with a bulk density of 1.5 g/ml, 0 % crop interception assumed.
Application rate	Worst case application: Oilseed rape and sugar beet: 0.1 + 0.2 kg/ha, calculated as one single application of 0.3 kg/ha

$PEC_{(s)}$ (mg/kg)	Single application PECcont(t) Oilseed rape, sugar beet	Single application PECtwa(t) Oilseed rape, sugar beet
Initial	0.40 mg/kg	0.40 mg/kg

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

Metabolite

Method of calculation	No major metabolites in addition to CO_2 Unidentified minor metabolites max. 7.7 % of AR at 20 ˚C. As no major soil metabolites of clopyralid were found in the degradation studies, the PECsoil for metabolites was not calculated. Not required.
Application rate	PECsoil for metabolites was not calculated. Not required.

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) ‡ (state pH and temperature)	pH 4, 50 °C: DT_{50} >1 year
	pH 7, 50 °C: DT_{50} >1 year
	pH 9, 50 °C: DT_{50} >1 year no hydrolytic degradation, clopyralid was the only component determined in the buffer solutions
Photolytic degradation of active substance and relevant metabolites ‡	Natural sunlight, outdoor experiment at 37.45 °N, DT_{50} ca 271 days, no photolytic degradation products in aqueous sterile buffer could be observed. Photolysis is not a significant route of degradation of clopyralid in waters.
Readily biodegradable (yes/no)	No: in the Modified Sturm Test the cumulative CO2 production of clopyralid was 5-10 % of the theoretical maximum after 27 days.
Degradation in water/sediment - DT_{50} water ‡ - DT_{90} water ‡	Two systems, first order kinetics: 128 – 167 days, mean = 148 d 425 – 556 days, mean = 491 d R^2 = 0.731 – 0.764 (n=2) (recalculated by the Notifier) DT_{50} 143 – 182 d, mean = 163 d R^2 = 0.81 in both systems (n=2) (calculated in original study report)
- DT_{50} whole system ‡ - DT_{90} whole system ‡	not determined, as clopyralid is mainly distributed in the water phase
Mineralization	CO_2 evolved 2.3 – 5.3 % of AR in 100 days at study end (n=2)
Non-extractable residues	Max 6.2 – 7.3 % of AR after 30 days, declined to 2.0 – 5.9 % of AR in 100 days at study end (n=2)

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

Distribution in water / sediment systems (active substance) ‡	Unchanged clopyralid: Whole system: 86.6 – 88.6 % of AR after 100 days Water phase: 56.0 – 67.2 % of AR after 100 days Sediment phase: maximum 23.8 – 30.6 % of AR after 100 days. DT_{50} in sediment not calculated.
Distribution in water / sediment systems (metabolites) ‡	No major metabolites could be determined. The extractable RA in water and sediment phases was mainly unchanged clopyralid + at least three unidentified minor metabolites with a combined maximum of 5.4 % of AR after 100 days.

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

Parent

Method of calculation	First order kinetics, mean DT_{50lab} of 148 days for dissipation from water phase. Spray drift: German drift tables, 90th percentile drift for row crops (e.g. cereals), 30 cm water depth. Run-off: 0.5 % of application rate from a 1 ha field into a 0.2 ha pond, 1 m deep, 50 % crop interception assumed. Drainflow: UK drainflow model, 30 cm x 1m ditch at the edge of the treated field, 1.9 % of applied dose assumed to be transported to drainage ditch in 10 mm of drain water, max rate of 100 + 200 g/ha with no degradation assumed between the applications, 50 % crop interception.
Application rate	Oilseed rape, sugar beet: 0.1 + 0.2 kg as/ha, calculated as single application of 0.3 kg as/ha Cereals: 0.15 kg as/ha Pasture: 0.24 kg as/ha
Main routes of entry	Spray drift, runoff, drainflow. **Drainflow** gives the highest PEC_{sw} values and should be used in the risk assessment for aquatic organisms.

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

$PEC_{(sw)}$ (µg/L)	Single application Actual With highest rate	Single application Time weighted average Oilseed rape, sugar beet	Single application Time weighted average Cereals	Single application Time weighted average Pasture
Initial (spray drift from 1 m)	2.770	2.770	1.385	2.216
Intial (run off)	0.375	0.375	0.188	0.300
Initial (**drainflow**)	21.9	21.9		
Short term 24h	(spray drift)	2.764	1.382	2.211
2d		2.757	1.379	2.206
4d		2.744	1.372	2.195
Long term 7d		2.725	1.363	2.180
14d		2.681	1.341	2.145
21d		2.638	1.319	2.111
28d		2.596	1.298	2.077
42d		2.515	1.257	2.012

Metabolite	Because no metabolites were found in the water/sediment study, the PEC_{sw} for metabolites has not been calculated nor required.

PEC (sediment)

Parent Method of calculation	Initial concentration of clopyralid in surface water is instantaneously partitioned between the water (30 cm depth) and a sediment layer (5 cm depth, bulk density 1.5 g/ml), adsorption K_d of 0.098 was derived from a mean K_{oc} value of 4.9 and assuming an organic carbon content of 2 %. PEC_{sw} initial = 2.770 µg/L resulting from spray-drift from 1 m no-spray zone following uses on oilseed rape and sugar beet, 1.385 µg/L following the use on cereals and 2.216 µg/L following the use on pasture. **Worst case**: PEC_{sw} initial = 21.9 µg/L resulting from **drainflow** and worst case uses on oilseed rape and sugar beet.

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

Application rate	Oilseed rape, sugar beet: 0.1 + 0.2 kg as/ha, calculated as single application of 0.3 kg as/ha Cereals: 0.15 kg as/ha Pasture: 0.24 kg as/ha

PEC$_{(sed)}$ (µg/kg)	Single application Actual Spray drift, use on oilseed rape and sugar beet	Single application Actual Spray drift, use on cereals	Single application Actual Spray drift, use on pasture	Single application Actual Drainflow, use on oilseed rape and sugar beet
Initial	0.265 µg/kg	0.132 µg/kg	0.212 µg/kg	2.095 µg/kg

Metabolite Method of calculation	Because no metabolites could be determined in the water/sediment study, the PECsed for metabolites has not been calculated nor required.

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Modelling calculation with FOCUSPELMO 2.2.2, six different applications run with all representative FOCUS ground water scenarios according to FOCUS guidance, 60 runs together to take into account the scenarios in combination with the locations relevant to the particular crop. First order kinetics assumed for clopyralid degradation with mean $DT_{50(lab)}$ of 38 days, following the correction for moisture content the input value of 36 days was used. For other input parameters mean K_{oc} of 4.9, mean Freundlich exponent of 0.761, water solubility of 143 g/L, vapour pressure of 1.33 x 10^{-3} Pa was used.
Application rate	1) Spring application to summer or winter oilseed rape, 200 g as/ha on March 1st, assuming 80 % crop interception covering BBCH 20-39 and 40-89. 2) Autumn application to summer or winter oilseed rape, 125 g as/ha on November 30th, assuming 40 % crop interception covering BBCH 10-19. 3) Spring application to sugar beet, 100 g as/ha on May 1st, followed by 200 g as/ha 21 days later, assuming 70 % crop interception covering BBCH 20-39.

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

	4) Spring application to spring or winter cereals, 125 g as/ha on March 1st, assuming 25 % crop interception covering BBCH 10-19. 5) Spring application to pasture, 240 g as/ha on Mach 1st, assuming 90 % crop interception, continuous crop. 6) Autumn application to pasture, 240 g as/ha on November 30th, assuming 90 % crop interception, continuous crop
PEC$_{(gw)}$	
Maximum concentration	Individual peak concentrations were not calculated. Highest 80th percentile annual average concentrations were achieved with autumn application on winter oilseed rape, 2.669 – 6.721 in all six representative scenarios
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	Leachate below 1 m depth: in 54 of the 60 runs the 80th percentile annual average concentration exceeded the trigger of 0.1 µg/L. **The only representative use scenarios with < 0.1 concentrations could be demonstrated as:** -spring application to summer oilseed rape in Porto (0.046) - (this simulation does not cover the GAPs proposed since BBCH 20-39 and 40-89 have been assumed), -spring application to sugar beet in Sevilla (0.090) - (this simulation does not covers the GAPs proposed since BBCH 20-39 have been assumed), -spring application to winter cereals in Sevilla (0.020) - (this simulation may be considered to cover the spring application to winter cereals in Southern EU), -spring application to pasture in Porto (0.077), Sevilla (0.004) and Thiva (0.020) - this simulation may be considered to cover the spring application to pastures in Southern EU). Higher tier modelling using mean DT_{50} values is required. From the data presented in the DAR, all autumn applications appeared to be unsafe with regard to ground waters.

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

Direct photolysis in air ‡	No data submitted nor required
Quantum yield of direct phototransformation	No data submitted nor required

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

Photochemical oxidative degradation in air ‡	Atkinson calculation using AOPWIN v.1.90 DT_{50} = 19.5 days
Volatilization ‡	BBA guideline: from plant surfaces: <u><</u>4 % in 24 hours
	BBA guideline: from soil: <2 % in 24 hours

PEC (air)

Method of calculation	Not required: clopyralid is not anticipated to be present in air in significant quantities. Expert judgement based on vapour pressure, dimensionless Henry's Law Constant and information on volatilisation from plants and soil.

$PEC_{(a)}$

Maximum concentration	negligible

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	Soil, surface and ground waters, air: clopyralid

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

Soil (indicate location and type of study)	No data provided nor required.
Surface water (indicate location and type of study)	Survey on monitoring programmes in 15 European countries: surface and ground waters, including some data on drinking waters. Surface water data on clopyralid was available in France, Germany, Norway, Sweden and the UK. Maximum concentrations of 10 in Sweden and 14 in UK were reported. (These values are more or less comparable to the PEC_{sw} values calculated for the monograph, e.g. 2.77 following spray drift or 21.9 following drainflow.) For drinking water, several cases of non-compliance with the drinking water standard of 0.1 have been reported in UK, where remedial measures were required in at least 100 water supply zones of two water companies, and at three sites in Germany.

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

Ground water (indicate location and type of study)	Survey described above: Clopyralid was analysed and found in groundwater in Denmark, Germany and the UK. The drinking water standard of 0.1 µg/L was exceeded in three samples in DK and up to three samples in the UK. The concentration of 0.1 µg/L was exceeded in 2 samples in Denmark.
Air (indicate location and type of study)	No data provided nor required

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	None according RMS proposal to ECB based on ecotoxicological assessment.

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

Appendix 1.6: Effects on non-target Species

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

Acute toxicity to mammals ‡	Rat: acute LD_{50} >5000 mg/kg body weight Rat: 13-week subchronic NOAEL 300 mg as/kg bw/day Dog: 12-month subchronic NOAEL 100 mg as/kg bw/day
Acute toxicity to birds ‡	Mallard duck: LD_{50} 1465 mg/kg body weight
Dietary toxicity to birds ‡	Bobwhite quail and mallard duck: 8 day LC_{50} >5000 mg/kg diet equivalent to 1033 mg as/kg bw/day (quail)
Reproductive toxicity to birds ‡	Mallard duck: NOEC 1000 mg/kg diet equivalent to 118 mg as/kg bw/day
	Rat: 2-year chronic NOAEL 50 mg/kg bw/day

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
1 x 0.240 kg/ha	pasture	Large grazing herbivorous bird	acute	98	10
1 x 0.150 kg/ha	Cereal shoots	Large grazing herbivorous bird	acute	156	10
1 x 0.300 kg/ha	Oilseed rape, sugar beet foliage	Large grazing herbivorous bird	acute	74	10
1 x 0.300 kg/ha	Oilseed rape, sugar beet	Small insectivorous bird	acute	90	10
1 x 0.300 kg/ha	Oilseed rape, sugar beet	Medium sized bird eating earthworms	acute	510	10
1 x 0.240 kg/ha	pasture	Small herbivorous mammal	acute	>106	10
1 x 0.150 kg/ha	Cereal shoots	Small herbivorous mammal	acute	>169	10
1 x 0.300 kg/ha	Oilseed rape, sugar beet foliage	Small herbivorous mammal	acute	>684	10
1 x 0.300 kg/ha	Oilseed rape, sugar beet	Small insectivorous mammal	acute	>1890	10

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
1 x 0.300 kg/ha	Oilseed rape, sugar beet	Small earthworms eating mammal	acute	>1368	10
1 x 0.240 kg/ha	pasture	Large grazing herbivorous bird	short term	>129	10
1 x 0.150 kg/ha	Cereal shoots	Large grazing herbivorous bird	short term	>206	10
1 x 0.300 kg/ha	Oilseed rape, sugar beet foliage	Large grazing herbivorous bird	short term	>113	10
1 x 0.300 kg/ha	Oilseed rape, sugar beet	Small insectivorous bird	short term	>114	10
1 x 0.300 kg/ha	Oilseed rape, sugar beet	Medium sized bird eating earthworms	short term	>360	10
1 x 0.240 kg/ha	pasture	Small herbivorous mammal	short term	12	10
1 x 0.150 kg/ha	Cereal shoots	Small herbivorous mammal	short term	19	10
1 x 0.300 kg/ha	Oilseed rape, sugar beet foliage	Small herbivorous mammal	short term	89	10
1 x 0.300 kg/ha	Oilseed rape, sugar beet	Small insectivorous mammal	short term	311	10
1 x 0.300 kg/ha	Oilseed rape, sugar beet	Small earthworms eating mammal	short term	82	10
1 x 0.240 kg/ha	pasture	Large grazing herbivorous bird	long term	28	5
1 x 0.150 kg/ha	Cereal shoots	Large grazing herbivorous bird	long term	44	5
1 x 0.300 kg/ha	Oilseed rape, sugar beet foliage	Large grazing herbivorous bird	long term	24	5
1 x 0.300 kg/ha	Oilseed rape, sugar beet	Small insectivorous bird	long term	13	5
1 x 0.300 kg/ha	Oilseed rape, sugar beet	Medium sized bird eating earthworms	long term	41	5
1 x 0.240 kg/ha	pasture	Small herbivorous mammal	Long term	8	5

Refinements of the risk to small herbivorous mammals:

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

-Real concentration in oilseed rape and sugarbeet foliage is lower than calculated, because there is 21 days between the two applications of 0.1 and 0.2 kg as/ha. After one week post application the residue is halved.

-Vertebrates are not anticipated to forage solely and not for longer periods on treated crops.

Therefore the risk is considered as acceptable.

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg as/L)
Laboratory tests				
Rainbow trout	EF-255	acute	LC_{50}	**53**
Rainbow trout	Clopyralid tech.	acute	LC_{50}	>99.9
Daphnia magna	EF-255	acute	EC_{50}	130
Daphnia magna	Clopyralid tech.	acute	EC_{50}	**>99.0**
Green alga	EF-255	acute	E_bC_{50}	47.6
Green alga	EF-255	acute	E_rC_{50}	77.4
Green alga	Clopyralid tech.	acute	E_bC_{50}	30.9
Green alga	Clopyralid tech.	acute	E_rC_{50}	**30.0**
Blue-green alga	Clopyralid tech.	acute	E_bC_{50}	127
Blue-green alga	Clopyralid tech.	acute	EC_{50}[1]	37.1
Duckweed	Clopyralid tech.	acute	EC_{50}	**89**
Fathead minnow	Clopyralid tech.	chronic	NOEC	10.8
Daphnia magna	Clopyralid tech.	chronic	NOEC	17
(*Daphnia magna*	EF-255	chronic	NOEC	7.0)
Chironomus riparius	Clopyralid	chronic	NOEC	50

1 = least squares linear regression of algal cell counts
The values signed with bold are used in the aquatic risk assessment

Microcosm or mesocosm tests
No data submitted nor required

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

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	TER	Annex VI Trigger
0.3 kg/ha	Oilseed rape, sugar beet	Rainbow trout	acute	2420	100
0.3 kg/ha	Oilseed rape, sugar beet	*Daphnia magna*	acute	4520	100
0.3 kg/ha	Oilseed rape, sugar beet	Algae	acute	1370	10
0.3 kg/ha	Oilseed rape, sugar beet	Duckweed	acute	4064	10
0.3 kg/ha	Oilseed rape, sugar beet	Fathead minnow	chronic	493	10
0.3 kg/ha	Oilseed rape, sugar beet	*Daphnia magna*	chronic	320	10
0.3 kg/ha	Oilseed rape, sugar beet	*Chironomus riparius*	chronic	2283	10

The acute and chronic TER values for aquatic organisms resulting from spray drift from 1 m distance are not reported here, because the risk is negligible even with the worst case drainflow PEC_{sw}. The spray drift TERs are ca. ten times higher compared to respective values resulting from drainflow.

Bioconcentration

Bioconcentration factor (BCF) ‡	Bluegill sunfish: <1.0 in 28 days
Annex VI Trigger:for the bioconcentration factor	100
Clearance time (CT_{50}) (CT_{90})	Not calculated (negligible)
Level of residues (%) in organisms after the 14 day depuration phase	negligible

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

Acute oral toxicity ‡	LD_{50} >100 µg/bee
Acute contact toxicity ‡	LD_{50} >98.1 µg/bee

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

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
0.24 kg as/ha	pasture	oral	<2.4	50
0.24 kg as/ha	pasture	contact	<2.4	50

Field or semi-field tests

No data is submitted nor required, because the laboratory toxicity of clopyralid to honey bees is low and no risk is anticipated.

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

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests ‡						
Aphidius rhopalosiphi	adult	EF-1136	0.010 0.200	Mortality Fecundity Mortality Fecundity	0.0 % 42 % 0.0 % **90 %**	30 %
Typhlo-dromus pyri	Proto-nymphs	EF-1136	0.010 0.200	Mortality Fecundity Mortality Fecundity	1.2 % 39.2 % 5.9 % 27.7 %	30 %
Chrysoperla carnea	2nd instar larvae	EF-1136	0.200	Mortality Fecundity	6.67 % no effect	30 %
Poecilus cupreus	adult	EF-1136	0.200	Mortality Feeding	0.0 % 18.28 %	30 %
Poecilus cupreus	adult	EF 255	0.120	Mortality Feeding	0.0 % 8.4 %	30 %
Aleochara bilineata	adult	EF 255	0.120	Mortality Fecundity	0.0 % no effect	30 %
Pardosa spp.	adult	EF-1136	0.120	Mortality Feeding	0.0 % 7.5 %	30 %

In-field HQ for *A. rhopalosiphi* and *T. pyri* is calculated from Application rate / LR_{50}
where the highest application rate is 300 g clopyralid/ha, and LR_{50} is in excess of the highest rate tested, 200g/ha. Hence in-field HQ = 300 /200 = 1.5, which is less than the current trigger of 2 for both sensitive indicator species according to the recommendation of ESCORT 2. As the in-field risk is acceptable, no off-field risk is anticipated and no risk mitigation methods are necessary.

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

Field or semi-field tests
No data submitted nor required

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

Acute toxicity ‡	LC_{50} >1000 mg/kg (technical clopyralid) LC_{50} >97.6 mg/kg (a.s. or PPP)
Reproductive toxicity ‡	NOEC $\geq$2.0 mg/kg

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

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
0.4 kg as/ha	oilseed rape, sugar beet	acute	>244	10
0.4 kg as/ha	oilseed rape, sugar beet	chronic	5	5

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

Nitrogen mineralization ‡	By day 28 the soil nitrate-nitrogen transformation rates at the 1x and 5x field rates of clopyralid differed by +4.6 % and +18 % from the control mean, respectively. These values are below the 25 % criterion of the effect as stated in the guideline OECD 216.
Carbon mineralization ‡	By day 28 the soil respiration rates at the 1x and 5x field rates of clopyralid differed by –2.0 % and –7.8 % from the control mean, respectively. These values are below the 25 % criterion of effect as stated in the guideline OECD 217.

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

Effects on other non-target organisms (flora and fauna) (Annex IIA, point 8.6)

Non-target plants	For *Avena sativa, Allium cepa, Cyperus esculentus, Brassica napus* and *Beta vulgaris* the 21 days EC_{50} based on foliar fresh weight reduction is >120 g as/ha and for *Glycine max* it is 25.4 g as/ha. For the most sensitive species *Glycine max* the TER of 7.7 is resulting from spray drift from 1 m distance following the single application rate of 120 g as/ha. From 1 m distance with application rate of 200 g as/ha the TER of 4.6 is close to the latest trigger of 5. At higher rates a no-spray zone of 5 m or drift reducing technology is adequate to reduce the risk at an acceptable level.

Effects on biological methods of sewage treatment (Annex IIA, point 8.7)

Activated sewage sludge respiration	No adverse effect at 100 mg/L. The 3 h EC_{50} for the inhibition of respiration of activated sludge is hence > 100 mg/L. The TER is >4566 using the worst case initial PEC_{sw} of 21.9 µg/L resulting from drainflow and therefore no risk is anticipated.

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	no classification

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

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

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

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