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

haloxyfop-P (haloxyfop-R)

finalised: 28 July 2006

SUMMARY

Although, in general, the Commission is using the ISO common names for the active substances, in this case the synonym haloxyfop-R (introduced by DOW AgroSciences) is used, which is in common use, but has no official status. However, to minimise confusion and misunderstandings the name haloxyfop-R is used in the EFSA conclusion, being aware that this is not in compliance with the general approach of the Commission.

Haloxyfop-R 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.

Denmark being the designated rapporteur Member State submitted the DAR on haloxyfop-R in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 21 November 2003. Following a quality check on the DAR, the peer review was initiated on 26 March 2004 by dispatching the DAR for consultation of the Member States and the sole applicant Dow AgroSciences. 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 on 27 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 April and May 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 9 June 2006 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as a herbicide as proposed by the applicant which comprises broadcast spraying to control annual and perennial

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

grasses in carrots, fodder legumes (peas and beans), rape seed, soy bean and sugar beet at a maximum application rate up to 0.104 kg haloxyfop-R per hectare. Only the use as herbicide was evaluated during the EU peer review process.
The representative formulated product for the evaluation was "EF-1400", an emulsifiable concentrate (EC), registered under different trade names in Europe.

Whether or not sufficient enforcement methods are available for monitoring purposes depends on the final residue definitions. The reason is that none of the submitted method is enantio selective. The residues are determined as a sum parameter of both, the *R*- and the *S*-isomer. This means that for the determination of haloxyfop-R no specific enforcement method would be available.
Furthermore, it should be noted that with the available analytical methods for food, soil and water it is not possible to differentiate between residue of the acid and its salts, esters and conjugates.
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.

The toxicological studies were generally performed with pure (>98%) racemic haloxyfop or haloxyfop-R methyl ester or with neat substances. The toxicokinetic studies indicate that absorbed methyl ester will rapidly be hydrolysed to the parent acid and the S-form haloxyfop present in racemic haloxyfop will instantaneously undergo stereochemical inversion to haloxyfop-R. Therefore, the various compounds used for testing are assumed to elicit the same systemic effects following administration and these effects can be attributed to haloxyfop-R. The absorption is rapid (> 80%) and the excretion extensive. The acute oral toxicity is moderate i.e. LD_{50} is around 300 mg/kg bw and the dermal toxicity low LD_{50}> 2000 mg/kg bw, proposed classification of Xn, R22 “Harmful if swallowed”. No acute inhalation toxicity studies are available. Neither racemic haloxyfop nor haloxyfop-R methyl ester was irritating to skin and haloxyfop-R methyl ester was not a sensitizer. Haloxyfop-R methyl ester is not irritating to the eye whereas racemic haloxyfop induced signs of irritation in the conjunctival sacs and iris and caused corneal opacity covering up to 100% of the cornea in all animals. Signs of irritation (corneal opacity) persisted for 21 days in un-rinsed eyes racemic haloxyfop is therefore irritating to the eye and the classification of Xi; R41 “Risk of serious damage to eyes” is proposed. The relevant short term NOAEL is 0.5 mg/kg bw/day based on the 1-year dog study which would also be said to cover the effects observed in the 90-day studies in the dog and monkey at 2 mg/kg bw/day.
There is no mutagenic or genotoxic potential for haloxyfop-R. Haloxyfop is not carcinogenic in the rat but there are hepatocellular adenomas in the highest dose in the mice associated with peroxisome proliferation.
No reproductive effects were observed at the highest dose level of 1 mg/kg bw/day, thus being a NOAEL for reproductive effects, the NOAEL for offspring toxicity is 0.065 mg/kg bw/day based on decreased body weight of f_{1a} pups after 21 days at 1 mg/kg bw/day.

The NOAEL for maternal effects is 7.5 mg/kg bw/day and the NOAEL for developmental toxicity is 7.5 mg/kg bw/day in the first study and 15 mg/kg bw/day in the second study.
No specific studies are available for the metabolites.
The acceptable daily intake (ADI) is 0.00065 mg/kg bw/day, the acceptable operator exposure level (AOEL) is 0.005 mg/kg bw/day and the acute reference dose (ARfD) is 0.075 mg/kg bw/day, with the safety factor of 100 applied.
The operator exposure was estimated using the standard models UK-POEM and the German model.
The dermal absorption is 7% and 12% for the concentrate and the diluted product, respectively. The AOEL is exceeded (169%) according to the UK-POEM even with PPE (coverall) but is below according to the German model if PPE (coverall and gloves) is applied (12%). The estimated worker and bystander exposure is below the AOEL.

To investigate the residue behaviour of haloxyfop-R in plants and livestock either the haloxyfop R-isomer or the unresolved isomeric mixture or ester variants of both compounds were used.
Plant metabolism was studied following foliar application to crops representing leafy crops, root vegetables, pulses and oilseeds. Irrespective of the ester variant or whether the racemic mixture or only the R-isomer was applied, the metabolism in all the studied crops was found to be similar commencing by a rapid and almost complete degradation to haloxyfop (R,S) very soon after application, followed by conjugation with carbohydrates and triglycerides. These conjugates appeared to be unstable under alkaline and acidic conditions, releasing haloxyfop (R,S) again.
Metabolism studies with goats and hens indicated that haloxyfop (R,S) is excreted unmetabolised by livestock animals. In tissue and organs residues were present as haloxyfop (R,S) in either form, free and conjugated.
Due to the lacking isomeric specificity of the pre-registration analytical methods any possible stereochemical inversion in either direction in food of plant and animal origin could not be detected, even though it is assumed based on available data in soil and in rats that if such inversion occurs it will be most likely from the S- to the R-isomer.
A sufficient number of residue trial data with haloxyfop-R methyl according to the GAP proposed for the representative uses is available to conclude the risk assessment for consumers and to propose MRLs. From crop rotation studies it can be concluded that no significant residue levels are expected in rotational and succeeding crops following application of haloxyfop-R methyl according to the critical GAP. The residue levels that could occur in food of animal origin when crops treated with haloxyfop-R methyl are fed to animals were assessed based on livestock feeding studies and MRLs have been proposed.
The dietary risk assessment performed for different consumer groups indicates that there are no chronic and acute concerns related to dietary exposure resulting from the representative uses assessed within the peer review procedure.

Soil degradation studies suggested a possible main degradation route for haloxyfop-R methyl ester under aerobic conditions. Haloxyfop-R methyl ester degraded rapidly (DT_{50} < 0.6 d at 20ºC) in six

soils to produce the acid metabolite haloxyfop-R[3] (maxima concentrations ranged from 53 to 91% AR), which further degraded to DE-535 pyridinol[4] (max. 29-52% AR). Other two metabolites, DE-535 pyridinone[5] and DE-535 phenol[6], exceeded the trigger value of 10% AR on a limited number of occasions: DE-535 pyridinone reached a maximum of 11.0% AR after 120 days, and DE-535 phenol with maximum concentration of 12.6% AR after 14 days. Final degradation ended up in minor unidentified metabolites, non-extractable soil residues (max. 44% AR after 90 days) and carbon dioxide (max. 35% AR after 90 days). Haloxyfop-R can be considered as very low to low persistent, DE-535 pyridinol as medium to high persistent, DE-535 phenol as moderate to high persistent and DE-535 pyridinone as high persistent.

Sorption characteristics indicated that haloxyfop-R, DE-535 pyridinol and DE-535 pyridinone are very high to high mobile in soil, whereas DE-535 phenol can be classified as low mobile. Haloxyfop-R and the metabolite trifluoroacetic acid exceeded the limit value of 0.1 µg/L on individual occasions in some lysimeter studies, but the annual average concentrations were < 0.1 µg/L for haloxyfop-R methyl ester and all its metabolites.

Because the calculation model for PECsoil was not consistent with the method used for the degradation rates values, soil concentrations at later time points for haloxyfop-R, DE-535 phenol and DE-535 pyridinone should be recalculated. However, the new PECsoil values will not have an impact on the risk assessment for terrestrial organisms as safe uses have been shown using the reliable initial PECsoil.

The hydrolysis rate of haloxyfop-R methyl ester was directly correlated with pH (stable at pH 4, DT_{50}= 43 days at pH 7 and DT_{50}= 0.63 days at pH 9). The photolysis of haloxyfop-R methyl ester and haloxyfop-R was investigated in pH 5 sterile buffer and natural water (pH 8.5). A new metabolite, with a chemical structure similar to dibenzofuran, was identified up to 18.6% AR in the sterile buffer system. Because a final conclusion on the ecotoxicological and toxicological relevance of this metabolite can not be drawn, the aquatic exposure of DE-535 furan needs to be addressed.

Two natural water-sediment systems under controlled laboratory conditions showed that haloxyfop-R methyl ester was rapidly hydrolyzed to haloxyfop-R, the concentrations of which were in the range of 63.8 - 81.5% AR after 1-30 days. At the same time the concentration of the metabolite DE-535 pyridinol increased up to 19.7% AR after 59 days. The same two metabolites were also found in the sediment phase up to 33.7% AR (haloxyfop-R) and 16.4% AR (DE-535 pyridinol). Haloxyfop-R methyl ester degraded rapidly in both the water and sediment phases with first order DT_{50} values < 0.3 days. The calculated DT_{50} values for haloxyfop-R ranged from 39.2 – 51.7 d (whole system) and from 31.5-54.6 d (water phase).

The available aquatic exposure assessment is appropriate for addressing the spray drift route on entry to surface water for haloxyfop-R methyl ester, haloxyfop-R and DE-535 pyridinol. Additional calculations were performed including a worst-case contamination contribution from run-off and drainage of 15% of the application rate.

[3] (R)-2-[4-((3-Chloro-5-(trifluoromethyl)-2-pyridinyl)oxy]phenoxy)propanoic acid
[4] 3-chloro-5-trifluoromethylpyridin-2-ol
[5] [5] 3-chloro-1-methyl-5-(trifluoromethyl)-2(1H)-pyridinone
[6] 4-(3-chloro-5-trifluoromethyl-2-pyridyloxyphenol

The available FOCUS groundwater modelling indicated that there is a high potential of groundwater contamination from the metabolites DE-535 pyridinol (80th percentile annual average concentrations: 0.55-2.87 µg/L) and DE-535 pyridinone (0.26-0.90 µg/L) under vulnerable situations for all the 9 FOCUS groundwater scenarios. However, the DT_{50} values used in the modelling were derived with a method not compatible with the method assumed by the PELMO model as recommended by the FOCUS group. Therefore, the values presented in this conclusion should be taken with caution and should be confirmed by an appropriate FOCUS groundwater modelling. Pending the outcome, an evaluation of the relevance of the metabolites following the guidance document on relevant metabolites has to be completed. In the case the trigger of 0.1 µg/L or 0.75 µg/L is exceeded there is a need to provide information on the toxicological properties and possibly consumer risk assessment.

Based on the available volatilisation experiment and the calculated atmospheric half-life, contamination of the air compartment and long range transport through air are not expected.

The first tier risk assessment for herbivorous and insectivorous birds resulted in TER values above the Annex VI trigger indicating a low risk. For medium herbivorous and insectivorous mammals the acute risk is considered to be low, while a first tier high long-term risk was identified. The MS experts did not accept a proposed refinement using a higher endpoint from a 16-week dietary study. It was agreed to use the endpoint of 1 mg/kg bw/day from a 2-generation reproduction study. Furthermore, since the half-life for residues in vegetation was observed to be longer than the default value, residue decline data for each crop should be used in the risk assessment. The resulting TER values are foreseen to be below the Annex VI trigger indicating a high risk, and the risk to mammals needs to be further addressed.

Haloxyfop-R methyl ester is very toxic to aquatic organisms, fish being the most sensitive group of organisms. Risk mitigation comparable to 5 m buffer zones is required to meet the Annex VI trigger. The risk to aquatic organisms from the surface water metabolites haloxyfop-R and DE-535 pyridinol is considered to be low, except for sediment dwelling organisms for which a reproduction study with *Chironomus riparius* using DE-535 pyridinol is required before a full conclusion can be drawn. No information on the toxicity of the photolysis metabolite DE-535 furan is available. If an assumption of ten times higher toxicity compared to haloxyfop-R methyl ester were applied, the resulting TER value would be below the Annex VI acute trigger. Thus data to address the toxicity of this metabolite to aquatic organism is considered necessary. Two metabolites were found in concentrations >0.1 µg/L in the FOCUS ground water modelling. DE-535 pyridinol is considered to be of no ecotoxicological relevance. A conclusion regarding the relevance of DE-535 pyridinone can only be drawn once available studies have been evaluated.

The risk to bees and other non-target arthropods is low. The risk to earthworms, other soil macro-organisms and soil micro-organisms from haloxyfop-R methyl ester and haloxyfop-R is considered to be low. However, the risk to soil organisms from exposure to the persistent soil metabolites DE-535 pyridinol, DE-pyridinone and DE-535 phenol needs to be addressed. The risk to biological methods

of sewage treatment is considered to be low. No evaluated studies are available to conclude on the risk to non-target plants.

Key words: haloxyfop-P, haloxyfop-R, 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. Although, in general, the Commission is using the ISO common names for the active substances, in this case the synonym haloxyfop-R (introduced by DOW AgroSciences) is used, which is in common use, but has no official status. However, to minimise confusion and misunderstandings the name haloxyfop-R is used in the EFSA conclusion, being aware that this is not in compliance with the general approach of the Commission. Haloxyfop-R is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating Denmark as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, Denmark submitted the report of its initial evaluation of the dossier on haloxyfop-R, hereafter referred to as the draft assessment report, to the EFSA on 21 November 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 26 March 2004 to the Member States and the main applicant Dow AgroScience 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 attended 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 of Consumer Protection and Food Safety (BVL) in Braunschweig, Germany, in April and May 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 9 June 2006 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 15 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 19 June 2006)

Given the importance of the draft assessment report including its addendum (compiled version of June 2006 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

By the time of the presentation of this conclusion to the EU-Commission, the rapporteur Member State has made available amended parts of the draft assessment report which take into account mostly editorial changes. Since these revised documents still contain confidential information, the documents cannot be made publicly available. However, the information given can basically be found in the original draft assessment report together with the peer review report which both is publicly available.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Haloxyfop-P is the ISO common name for (*R*)-2-{4-[3-chloro-5-(trifluoromethyl)-2-pyridyloxy]phenoxy}propionic acid (IUPAC). The unresolved isomeric mixture of this substance has the common name haloxyfop. It should be noted that the name haloxyfop-R (synonym introduced by DOW AgroSciences) is in common use, but has no official status. However, to minimise confusion and misunderstandings the name haloxyfop-R is used in the EFSA conclusion, being aware that this is not in compliance with the general approach of the Commission. Due to the fact that the methyl ester, a variant of haloxyfop-R, is used in the formulated product, it should be noted that the evaluated data belong to the variant haloxyfop-R-methyl, unless otherwise specified.

Haloxyfop-R and haloxyfop-R-methyl, respectively, belong to the class of aryloxyphenoxyproponic herbicides (commonly called "FOP") such as clodinafop, fenoxaprop-P and fluazifop-P. Haloxyfop-R is taken up via leaves and roots and hinder the *de novo* synthesis of fatty acids by inhibition of the enzyme Acetyl-CoA carboxylase (ACCase).

The representative formulated product for the evaluation was "EF-1400", an emulsifiable concentrate (EC), registered under different trade names in Europe.

The evaluated representative uses as post emergent herbicide comprise broadcast spraying to control annual and perennial grasses in carrots, fodder legumes (peas and beans), rape seed, soya bean and sugar beet at a maximum application rate of 0.104 g haloxyfop-R-methyl per hectare.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of the haloxyfop-R methyl ester as manufactured should not be less than 940 g/kg (at least 96% enaniomeric excess)[7].
At the moment no FAO specification exists.
The technical material contains no relevant impurities.

It should be noted that the meeting of experts had required clarification with respect to the confirmation of the identity of the impurities and the used reference standards. The RMS has provided an addendum to Volume 4, recently (June 2006). According to the assessment of the RMS, the data are acceptable to address the requirements (the identity is determined primarily by MS). However, this was neither peer reviewed nor discussed in a meeting of experts.
In the case of the used standards, the announced justification for the standards was not yet submitted to the RMS.

The content of haloxyfop-R in the representative formulation is 104 g/L (pure) and 108 g/L (pure) as haloxyfop-R methyl ester, respectively.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of haloxyfop-R or the respective formulation.

[7] It should be noted that the technical material contains small amounts of the inactive *S*-isomer (*S*)-2-{4-[3-chloro-5-(trifluoromethyl)-2-pyridyloxy]phenoxy}propionic acid. However, the COM has confirmed for an comparable situation (1,3-dichloro-propene) that Article 2 of Commission Regulation 2076/2002 is not applicable in a similar situation.

The main data of haloxyfop-R and its methyl ester regarding the identity 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 haloxyfop-R methyl in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.
Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.

Whether or not sufficient enforcement methods are available for monitoring purposes depends on the final residue definitions. The reason is that none of the submitted method is enantio selective. The residues are determined as a sum parameter of both, the *R*- and the *S*-isomer. This means that for the determination of haloxyfop-R no specific enforcement method would be available.
Depending on the final residue definition for soil and water (ground and surface) it could be necessary to require further data. It should be noted that for the mentioned metabolites only a methods for the DE-535 pyridinol metabolite[8] were submitted, but these needs to be re-evaluated, if appropriate.
Furthermore, it should be noted that with the available analytical methods for food, soil and water it is not possible to differentiate between residue of the acid and its salts, esters and conjugates.
The methodologies used are GC with MS or EC detection. None of them is enantio selective. A multi-residue method like the Dutch MM1 or the German S19 is not applicable to due the nature of the residues.

The discussion in the meeting of experts (EPCO 25, May, 2005) on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material certain physical and chemical properties of haloxyfop-R and the preparation, and the analytical methods.
The required clarification concerning the *n*-octanol/water partition coefficient was provided by the rapporteur Member State in the evaluation table only (rev. 2-0, 30.05.2006).
The assessment of the rapporteur Member State that the recently submitted analytical method (addendum B.5, September 2005) is sufficient to fulfil the requirements of the Baby-Food-Directive was neither peer-reviewed nor discussed in a meeting of experts.

2. Mammalian toxicology

Haloxyfop-R was discussed at EPCO experts' meeting for mammalian toxicology (EPCO 23) in May, 2005. The studies were generally performed with pure (>98%) racemic haloxyfop or haloxyfop-R methyl ester dissolved in corn oil (or acetone/corn oil), or with neat substances. The toxicokinetic

[8] DE-535 pyridinol: 3-chloro-5-trifluoromethylpyridin-2-ol

studies indicate that absorbed methyl ester will rapidly be hydrolysed to the parent acid (see below) and the S-form haloxyfop present in racemic haloxyfop will instantaneously undergo stereochemical inversion to haloxyfop-R. Therefore, the various compounds used for testing are assumed to elicit the same systemic effects following administration and these effects can be attributed to haloxyfop-R.

2.1 ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

The absorption is rapid and the excretion extensive, studied in rats, monkey and humans. The oral absorption was discussed at the experts´ meeting and it was confirmed that the major route of excretion was via the bile > 80%, and no correction factor was needed to be applied to the AOEL. Haloxyfop is distributed primarily to plasma, liver and kidneys, there is no accumulation. The toxicokinetic pattern seems to be similar either if it is a racemic mixture of halxyfop acid or methyl ester. In addition, racemic mixtures (50:50 ratios of R- and S-enantiomers) were rapidly stereoisomerised to the R-enantiomer in rats which was confirmed by the experts. The major metabolites were haloxyfop acid and conjugates of haloxyfop acid.

2.2 ACUTE TOXICITY

Three studies (two in rats, one in mice) are available regarding acute oral toxicity and the LD_{50} is around 300 mg/kg bw for haloxyfop-R methyl ester or the racemic mixture. The dermal toxicity is low LD_{50}> 2000 mg/kg bw. No acute inhalation toxicity studies not available but is not required.
Neither racemic haloxyfop nor haloxyfop-R methyl ester was irritating to skin and haloxyfop-R methyl ester was not a sensitizer. Haloxyfop-R methyl ester is not irritating to the eye whereas racemic haloxyfop induced signs of irritation in the conjunctival sacs and iris and caused corneal opacity covering up to 100% of the cornea in all animals. Signs of irritation (corneal opacity) persisted for 21 days in un-rinsed eyes, but were reversible at 4 to 10 days in rinsed eyes. Racemic haloxyfop is therefore irritating to the eye.

Classification for acute toxicity is needed and the proposed risk phrases are: Xn, R22 "Harmful if swallowed". Xi; R41 "Risk of serious damage to eyes" is warranted for racemic haloxyfop and haloxyfop-R whereas no classification is warranted for haloxyfop-R methyl ester.

2.3 SHORT TERM TOXICITY

Eleven studies on short-term toxicity, 10 with oral administration of racemic haloxyfop and one with oral administration of haloxyfop-R (the 16-week study in rats), are available. Generally, the studies were not performed in accordance with modern guidelines for toxicity testing.

Target organ, in rodents, dogs and monkeys, is the liver (increased organ weight, gross pathology observations and histopathological changes being more pronounced in rodents compared to the dog and the monkey). Haloxyfop is a peroxisome proliferator in rodent livers and the liver effects have therefore been discussed to be irrelevant with respect to risk assessment in humans. However, electron microscopic examinations of the liver from dogs and monkeys revealed no indications of

peroxisome proliferation in these species despite the marked increase in liver weight. This indicates that haloxyfop also has a potential of inducing effects in the liver, which are not related to peroxisome proliferation. This issue was discussed at the experts´ meeting and the peroxisome proliferation was concluded to be rodent specific and not a concern for human toxicity, but that the effects on livers should be considered as an adverse effect and of relevance when setting the reference values.

The relevant short term NOAEL is 0.5 mg/kg bw/day based on the 1-year dog study which would also be said to cover the effects observed in the 90-day studies in the dog and monkey at 2 mg/kg bw/day.

2.4 GENOTOXICITY

In the DAR the genotoxic properties were studied in 9 *in vitro* studies (of which two Ames tests) and one *in vivo* test with racemic haloxyfop or haloxyfop-R. The purity ranged between 98.4% and >99% (one with no information). As the minimum purity is 94%, the problem whether the impurity DE-535 pyridinone (3 g/kg) was included in the tested batches was discussed during the experts´ meeting. After the meeting the rapporteur Member State has prepared an addendum (June, 2005) with further information which has been discussed through a written procedure (October, 2005). Since most of the studies are old (performed during 1980´s) analytical profiles were neither requested or are not available. However, it is still unclear which technical material and impurity profile has been used. Anyhow, it is stated that the impurity is present in one batch (TSN 101748) at a level of 0.88 g/kg which was used in the *in vitro* chromosome aberration test where a negative result was obtained.

The overall conclusion is that there is no mutagenic or genotoxic potential for haloxyfop-R.

2.5 LONG TERM TOXICITY

Two long term studies (2-year) are available one in the rat and one in the mouse.
Racemic haloxyfop was not carcinogenic to rats. The systemic NOAEL is 0.065 mg/kg bw/day based on effects on the liver, increased relative liver and kidney weights and histopathological changes. The NOAEL for neoplastic effects in rats is 0.1 and 1 mg/kg bw/day in males and females, respectively.
In mice, a linear trend for increased hepatocellular neoplasms was observed at the 0.065 mg/kg bw/day dose level but the incidences were within the historical control data. However, a statistical increased number of hepatocellular carcinomas in high dose females (i.e. 0.6 mg/kg bw/day) were noted which was slightly above the historical control data and was explained by the peroxisome proliferator mechanism by the rapporteur Member State. The NOAEL for neoplastic effects in mice is 0.065 mg/kg bw/day. In mice, treatment-related effects were only observed in the liver slight increase in weight, and histopathological changes of high dose animals; the NOAEL for chronic, non-neoplastic effects is 0.065 mg/kg bw/day.

In conclusion, haloxyfop is not carcinogenic in the rat but there are hepatocellular adenomas in the highest dose in the mice.

2.6 REPRODUCTIVE TOXICITY

Two multigeneration studies and five developmental studies are available.

No reproductive effects were observed at the highest dose level of 1 mg/kg bw/day and thus this is a NOAEL for reproductive effects which is the same as for parents as no adverse effects were observed. The NOAEL for offspring toxicity is 0.065 mg/kg bw/day based on decreased body weight of f_{1a} pups after 21 days at 1 mg/kg bw/day.

In the three-generation study in rats the NOAEL for reproductive effects is 1 mg/kg bw/day. At this dose level, effects were observed in the liver of adult animals and in the kidneys from 0.05 mg/kg bw/day; the liver weights in weanlings at 1 mg/kg bw/day tended to be increased as well. The effects in the kidneys and weanling livers were minimal and not considered to be adverse. The parental NOAEL in this study is 0.05 mg/kg bw/day based on increased liver weights observed at the highest dose level.

Developmental toxicity was studied in rats and in rabbits. In range finding developmental studies in rats and rabbits, racemic haloxyfop administered during organogenesis elicited maternal and foetal toxicity in rats at daily doses from 10 mg/kg bw/day and maternal toxicity in rabbits at 25 mg/kg bw/day.

In rats racemic haloxyfop exhibited maternal toxicity at daily doses of 7.5 mg/kg bw during organogenesis, but was not toxic to the foetuses. The NOAEL for maternal toxicity is 1 mg/kg bw/day and for developmental toxicity 7.5 mg/kg bw/day.

In two studies in rabbits, maternal deaths occurred at the highest dose level (20 or 15 mg/kg bw/day, respectively) of racemic haloxyfop; no other signs of toxicity in the dams were recorded. In one of the studies, embryotoxicity (increased incidence of resorbed implantations) was observed at the highest dose level of 20 mg/kg bw/day whereas no developmental effects were observed in the other study at the highest dose level of 15 mg/kg bw/day. The NOAEL for maternal effects is 7.5 mg/kg bw/day in both studies; the NOAELs for developmental toxicity is 7.5 mg/kg bw/day in the first study and 15 mg/kg bw/day in the second study.

2.7 NEUROTOXICITY

No studies were submitted. No evidence of neurotoxic potential is seen in the toxicological studies. No specific studies are required.

2.8 FURTHER STUDIES

Specific studies on peroxisome proliferation

In the DAR, eights studies (from 1986 to 2002) are available to evaluate the proliferation of hepatocellular peroxisomes in various mammalian species with or without recovery period(s), or in cultured (primary) mammalian hepatocytes *in vitro*.

The results demonstrate that haloxyfop is a peroxisome proliferator in rats (*in vivo*) and mice (*in vivo, in vitro*), but not in human primary cell culture, guinea pigs, dogs or monkeys, It was demonstrated that changes resulting from 4 week administration were almost totally reversible in rats and mice within a 4 week recovery period. It was shown that other species as the dog and monkey were less sensitive to the increased peroxisomal volume density. Also, the well known positive control for peroxisome proliferation, WY14,643, failed to stimulate peroxisome proliferation in guinea pigs indicating an essentially non-responsive nature of guinea pig liver to the peroxisome proliferating effect.

The *in vitro* studies with cultured hepatocytes from mouse, guinea pig, and human showed that mouse hepatocytes were very affected (induction of the peroxisomal marker enzyme activity). However, haloxyfop (or the positive control) did not stimulate the peroxisome proliferation phenotype in primary cultures of human hepatocytes or in cultured guinea pig hepatocytes.

Thus, it can be concluded that haloxyfop acts as a peroxisome proliferator in rodents but not in non-rodents. This proposed mechanisms and argumentation was agreed by the experts although direct effects on the liver should be considered as adverse, see also 2.3 (and 2.5).

Metabolites

No specific studies are available.

EFSA note: Pending the outcome of the new FOCUS ground water modeling there might be a need to address the toxicological properties of metabolites (see 4.2).

Impurity

DE-535 pyridinone, no specific toxicological studies are available. It has been tested (0.88 g/kg) in an *in vitro* genotoxicity test with negative outcome (see 2.4).

2.9 MEDICAL DATA

No information is available in the DAR.

EFSA note: this is a data gap and was identified after the experts´ meeting.

2.10 ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) and ACUTE REFERENCE DOSE (ARfD)

ADI

The ADI is based on liver effects and the NOAEL is 0.065 mg/kg bw/day from the 2-year studies in rats and mice and two-generation study in rats. This was discussed and agreed at the experts´ meeting.

EFSA note: The margin of safety to the hepatocellular carcinomas observed in female mice at 0.6 mg/kg bw/day is approximately 1000.

The ADI is 0.00065 mg/kg bw/day, with the safety factor of 100 applied.

AOEL

Initially, the rapporteur Member State proposed an AOEL of 0.02 mg/kg bw/day based on the NOAEL from the 13-weeks study in monkeys, safety factor of 100.

The AOEL was discussed at the experts´ meeting and in accordance to the discussion of relevant short term NOAEL, the experts agreed to base the AOEL on the NOAEL of 0.5 mg/kg bw/day from the 1-year dog study. The need for possible correction for oral absorption was also discussed and could not be concluded at the experts´ meeting but was agreed afterwards (October, 2005) in written procedure that the oral absorption was > 80% (see 2.1) and no correction needed.

The AOEL is 0.005 mg/kg bw/day, with the safety factor of 100 applied.

ARfD

The ARfD, confirmed at the experts´ meeting, is based on the maternal NOAEL of 7.5 mg/kg bw/day from the developmental toxicity study in rabbits.

The ARfD is 0.075 mg/kg bw/day, with the safety factor of 100 applied.

2.11 DERMAL ABSORPTION

Two *in vivo* studies on the rat are available on the DAR, they are both performed with EF-1400 and this specific batch contained 111 g/L (nominal 108 g/L) of haloxyfop methyl ester. EF-1400 is the formulation code for Gallant Winner and Gallant Super.

Initially in the DAR the rapporteur Member State proposed 3% and 6% for the concentrate and dilution respectively based on results from the two *in vivo* studies and compensating from results obtained from a human toxicokinetic study (B.6.1 in the DAR).

At the experts´ meeting it was agreed that the human toxicokinetic study was neither scientifically valid with respect to exposure and sampling nor appropriate to make such compensation however, the picture was not complete for the *in vivo* study and the rapporteur Member State was asked to provide clarifications and further data on the distribution of the compound and the open point was not concluded.

After the experts´ meeting the discussion continued in a written procedure (October 2005) where the rapporteur Member State (addendum, June 2005) as well as notifier provided further information It was agreed by the experts that it was reasonable to assume the amount of haloxyfop still retained in skin (after 24 hours) would be systematically available and to apply the dermal absorption values of 7% for concentrate and 12% for the spray dilution.

2.12 EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product is Gallant Winner/Super (EF-1400) which is a emulsifiable concentrate containing 104 g/L of haloxyfop. The uses are carrot, fodder legumes, rapeseed, soya bean and sugar beet, maximum application rate is 0.104 kg/ha with tractor mounted broadcast sprayer.

Operator exposure

The operator exposure was estimated using the standard models UK-POEM and the German model. Since the AOEL and dermal absorption values were changed during the experts´ meeting (see 2.10 and 2.11), the risk assessment needed to be revised. The rapporteur Member State provided new calculations however, these were only based on the new AOEL, and not the correct dermal absorption values (addendum April 27, 2006).

EFSA note: At the experts´ meeting it was decided that the dermal absorption was 7% and 12% for the concentrate and the diluted product, respectively. Thus, recalculations were necessary and were provided during the Working group Evaluation meeting in June 2006 and are presented in the table below.

The AOEL is exceeded according to the UK-POEM even with PPE (coverall) but is below according to the German model if PPE (coverall) is applied.

Estimated exposure presented as % of AOEL (0.005 mg/kg bw/day), according to calculations with the German and UK-POEM model. The default for body weight of operator is 70 kg and 60 kg, and the treated area is 20 ha and 50 ha, respectively for the German and UK model.

Model	No PPE	Gloves M/L	Gloves M/L, A	Gloves M/L gloves + coverall A
German model	246%	147%	121%	12.2%
UK-POEM	1117%	899%*	-	169%

PPE (personal protective equipment), M/L: mixing and loading, A: application, * including coverall

Worker exposure

In the DAR, an estimation of the worker exposure is presented based on the AOEL (0.02 mg/kg bw/day) and a dermal absorption value for the formulation of 6% proposed by the rapporteur Member State, which were altered after discussion with the experts to 0.005 mg/kg bw/day and 12%, respectively.

It is assumed that the worker doesn't wear any PPE and the body weight is 70 kg. The estimated deposit of the active is based on values from Poppendorf (1992) and a leaf area index according to van Hemmen (1992). The range of exposure is between 0.006 to 0.03 mg/kg bw/day which is below the AOEL. In the DAR, the dermal absorption value of 6% is considered which results in a systemic exposure of 0.00033 mg/kg bw/day to 0.002 mg/kg bw/day.

EFSA note: The estimated worker exposure needed to be recalculated in accordance to revised AOEL and dermal absorption values. Recalculations were provided during the Working Group Evaluation meeting in June, 2006 and are available in the final addendum.

The estimated worker exposure is below the AOEL (maximum exposure up to 77% of the AOEL).

Bystander exposure

Recalculations of estimated bystander exposure, based on the revised AOEL and dermal absorption value, were provided during the Working Group Evaluation meeting in June, 2006 and are available in the final addendum. The estimated exposure is below the AOEL (less than 3%).

3. Residues

Haloxyfop-R was discussed at EPCO experts' meeting for residues (EPCO 24) in May 2005 in Braunschweig (Germany).

The residue behaviour of haloxyfop-R was studied with either the *R*-isomer or the unresolved isomeric mixture haloxyfop (isomer ratio *ca* 1:1) or with their ester variants respectively. The analytical methods utilised in all the residue tests and studies have not been specific for haloxyfop-R and therefore no differentiation between *R*- and *S*-isomer was possible. Thus, always the sum of both haloxyfop isomers was determined, irrespective of their ratio present[9], and possible stereo-isomerisation reactions (in either direction) could therefore not be detected.

However submitted data on investigation of enantiomer ratios in soil indicate that the S-isomer of haloxyfop is almost completely inverted to the R-isomer within a short period of time, presumably mediated by the soil microflora. Furthermore, results based on analysis of urine and faeces in a rat study, investigating the conversion between the two isomers, indicated that the S-isomer of haloxyfop undergoes rapid and nearly complete conversion to the R-isomer in the animal body. Whether the results found in soil and rats might be assignable to plants or livestock was not further investigated. It has been assumed by RMS that if any isomeric conversion following application to plants occurred it would most likely be the one from the S-isomer into the R-isomer. Moreover it was supposed that the racemic mixture was stereo-isomerised to the R-enantiomer also in livestock animals as observed in the rat. ECPO 24 considered that based on the information from rat metabolism it can be concluded that results from livestock studies with the racemic mixture are suitable to extrapolate to the residue behaviour of haloxyfop-R in livestock.

Since no particular distinction could be made between the isomers analysis and thus the extend of any potential isomerisation is not known in plants and livestock, the results of the studies are presented as haloxyfop (*R,S*) in the section of residues below, but not necessarily referring to an ratio 1:1 of the two isomers as present in the active substance haloxyfop.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

Metabolism studies were conducted with haloxyfop-R methyl ester in lettuce and sugar beet, and with different variants of the racemic mixture of haloxyfop (methyl, butyl or ethoxyethanol ester,

[9] Haloxyfop-R technical material contains also small amounts of the S-isomer

respectively) in soybean and cotton plants. The studies cover three different crop groups, i.e. leafy crops, root vegetables and pulses/oilseed.

After foliar spraying to lettuce and sugar beet, haloxyfop-R-methyl is rapidly degraded to haloxyfop *(R,S)* which was present in these crops at harvest at *ca* 55% and 30% of the total residue (TRR). Further conjugation of haloxyfop *(R,S)* with glucose and other carbohydrates was observed in these crops. No other metabolites were identified.
Regardless of whether methyl-, n-butyl- or ethoxyethanol-esters of haloxyfop were applied to leaves of soya plants, all esters were degraded to haloxyfop *(R,S)* in a short time after application. After two days less than 20% TRR were still present as haloxyfop *(R,S)* ester. After a foliar treatment of soya plants with haloxyfop butyl labelled in two different positions no differences were apparent between the two labels in neither the level nor the nature of the residues. In none of the studies there was evidence for decomposing of the oxygen bridge between the two ring molecules. The level of free haloxyfop *(R,S)* decreased with time while the level of conjugated haloxyfop *(R,S)* increased. In the fatty part of the soya bean haloxyfop *(R,S)* is esterified into triglycerides. Similar results were found in a study on metabolism of haloxyfop butyl in cotton plants.

The metabolism in all the studied crops was found to be similar, irrespective of the ester variant or whether the racemic mixture or only the R-isomer was applied. Haloxyfop esters and haloxyfop-R methyl are metabolised to haloxyfop *(R,S)* almost immediately after application and no or only very small amounts of ester may be detected in any plant parts.
Haloxyfop *(R,S)* was found to be further conjugated with carbohydrates, or with triglycerides in oil-containing -plant parts. These conjugates can be cleaved by alkaline hydrolysis and also by the acidic conditions as found in the stomach.
As the extraction in the analytical methods used is carried out under alkaline conditions releasing haloxyfop *(R,S)* from esters or conjugates, they are included in the residue finally determined as haloxyfop *(R,S).*

RMS considered it unlikely that significant amounts of the S-isomer will be present on the plants when haloxyfop-R is applied. Even though it was not investigated, based on the information available it is considered unlikely that in plants the R-isomer is inverted to the S-isomer when haloxyfop-R is applied. Available data on investigation of enantiomer ratios in soil indicate that the S-isomer of haloxyfop independent of the amount present is almost completely inverted to the R-isomer within a short period of time, presumably mediated by the soil microflora.

On this background it was concluded that in relation to the evaluation of haloxyfop-R, used in the formulated product as the variant haloxyfop-R methyl, the residue in plants should be defined as sum of haloxyfop-R methyl, haloxyfop-R (including the anionic form) and its conjugates expressed as haloxyfop-R for risk assessment purposes. Based on the information available and evaluated the proposed residue definition could be applied analogously if authorisation of other ester variants of haloxyfop-R such as butyl or ethoxyethanol-ester were sought.

The plant residue definition for monitoring was accordingly proposed as sum of haloxyfop-R methyl ester, haloxyfop-R (including the anionic form) and its conjugates expressed as haloxyfop-R.
From the toxicological evaluation it was assumed that regardless whether haloxyfop or haloxyfop-R was used for toxicological testing both compounds elicited the same systemic effects following administration (refer to point 2) Moreover due to the lacking isomeric specificity of the pre-registration analytical method any possible stereochemical inversion in either direction in food of plant and animal origin could not be detected, even though it is assumed that if such inversion occurs it will be most likely from the S- to the R-isomer. For the reasons given above and in consistency with previous conclusions it is proposed by EFSA to optionally define the residue for monitoring purposes as sum of haloxyfop *(R,S)* methyl ester, haloxyfop *(R,S)* (including the anionic form) and its conjugates expressed as haloxyfop *(R,S)*. It is noted that this proposal does not necessarily refer to a ratio 1:1 of the two isomers.

A sufficient number of residue trial data with haloxyfop-R methyl according to the GAP proposed for the representative uses is available. All samples were analysed with validated methods (but not isomer-specific) and the results were supported by acceptable storage stability data. The residue was determined as haloxyfop *(R,S)*, following of conversion of potentially present esters and conjugates to haloxyfop*(R,S)* under alkaline conditions, with a limit of quantification (LOQ) of 0.05 mg/kg.
Sufficient data from trials in carrots, soybeans, legumes and sugar beet is available to conclude the risk assessment for consumers and to propose MRLs. The data base on oil seed rape is complete for Northern Europe but is limited for Southern Europe (three trials only). All residues with one exception (N-EU: 0.07 mg/kg) were found to be below LOQ of 0.05 mg/kg. EPCO 24 considered whether is would be necessary to complete the data base for the South to assure a reliable risk assessment and/or MRL proposal. It was acknowledged by the meeting that with further trials the possibility of finding residues above the LOQ might increase. Based on the proposed GAP, an expected interval between application and harvest of more than 200 days and the results found in Northern EU trials, the experts considered it not very probable that further residue trials in the South will lead to results exceeding the proposed MRL of 0.1 mg/kg, even though few might possibly exceed the LOQ of 0.05 mg/kg.

Processing data on sugar beet shows that haloxyfop *(R,S)* residues are not concentrated in white sugar, raw juice and pressed pulp, but concentrated about 3-fold in green syrup. In molasses and molasses pulp processing factors were estimated to be about 18 and 8, respectively.
For soya beans and rapeseeds processing factors were determined for meal, refined and crude oil. While processing factors for refined and crude oil were comparable within the same study they differed markedly (0.4-2.2) between the individual studies conducted.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

To address the potential incorporation of soil residues into succeeding and rotational crops a confined accumulation study on rotational crops was conducted with radio labelled haloxyfop butyl ester in Michigan, USA. Haloxyfop butyl was applied to bare soil at a rate corresponding to 0.56 kg a.i./ha

haloxyfop and aged in the soil for 30 days before planting wheat, soya beans, leaf lettuce, carrots and turnips. Assuming an almost complete inversion of the haloxyfop S-enantiomer to the R-enantiomer within 7 days as indicated by experimental data on soil treated with haloxyfop *(R,S)* methyl the application rate in the study corresponds to *ca* 5 times the proposed application rate for haloxyfop-R. Crops were grown to maturity and samples were collected at normal harvest (49-115 DAT). Only in soya bean forage and in wheat straw total residues (TRR) exceeded 0.01 mg/kg, amounting to 0.07 mg/kg and 0.02 mg/kg in these matrices, respectively. Due to the low levels attempts to isolate and characterise these radioactive residues were unsuccessful.

In a field accumulation study on rotational crop (USA) haloxyfop methyl was applied at a rate of 280 g a.i./ha and 560 g a.i./ha, respectively, to plots planted with soya bean and cotton. Approximately at 30 and 120 DAT the primary crops were removed and lettuce, sugar beets and wheat were planted as rotational crops. The residues were determined as haloxyfop *(R,S).* No residues were detected in lettuce, sugar beet roots and tops and in wheat grain, however residues were detected in wheat forage samples and straw samples but they were all at or below the lowest validated concentration (LOQ) of 0.01 mg/kg and 0.02 mg/kg respectively. Considering the higher application rates used in these trials when compared with the proposed critical GAP (*ca* 2N and 4N, respectively) it can be concluded that no significant residue levels are expected in rotational crops following application of haloxyfop-R methyl according to the critical GAP. Even though situated outside Europe, the study locations were considered to adequately cover the climate conditions both in the northern and southern part of Europe.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Metabolism studies were conducted in lactating goats and laying hens. In both studies the test material was haloxyfop (unstated stereochemistry) since the variant (methyl ester) degrades very rapidly and haloxyfop *(R,S)* is the most pertinent compound found on plants i.e. potential feed items.

When lactating goats were dosed with radioactive labelled haloxyfop more than 89% of the radioactivity was excreted via the urine and *ca* 2% via faeces. Administered haloxyfop was rapidly and almost completely absorbed and excreted unmetabolised (as haloxyfop *(R,S)*) mainly via the urine. Only low levels of haloxyfop *(R,S)* were found in tissues and milk (0.5% and 3% administered dose, respectively). Most of the radioactivity in milk was present in the milk fat. In edible tissues from goats the highest amount was found in kidney followed by liver, muscle and fat. In liver and kidney only parent haloxyfop *(R,S)* was detected while in fat haloxyfop *(R,S)* was found as conjugate and in muscle it was not possible to determine any metabolites due to low content of radioactivity. Residues in liver and kidney were present as haloxyfop *(R,S)* while the residues in milk occurred as haloxyfop *(R,S)* incorporated into lipids (triglycerides) as esters, from where haloxyfop *(R,S)* could be released by alkaline hydrolysis or enzyme treatment.

When ^{14}C- haloxyfop was fed to laying hens about 86% of the radioactivity was eliminated through excreta. In eggs haloxyfop *(R,S)* is build into the triglycerides of the egg lipids. In kidney and liver haloxyfop *(R,S)* is partly found as conjugates.
In eggs most of the radioactivity was found in egg yolk and almost 100% of the radioactivity consisted as triglyceride conjugates of haloxyfop *(R,S)* from where it was be released by alkaline hydrolysis or enzyme treatment. In liver and kidney from chickens haloxyfop *(R,S)* and conjugates were found. Haloxyfop *(R,S)* was released from those conjugates by alkaline treatment. No further identification of the conjugates was carried out. In chicken fat no haloxyfop *(R,S)* was found after extraction but after alkaline treatment of the extract haloxyfop *(R,S)* was found, which means that haloxyfop *(R,S)* in chicken fat consisted of conjugates. No further identification of the conjugates was carried out.

Resulting from the evaluation of both, plant and livestock data and under the assumption of comparability of rat and livestock metabolism in terms of the occurrence of stereochemical inversion only towards haloxyfop-R it is proposed to define the residue for both enforcement and risk assessment for products of animal origin as sum of haloxyfop-R (including anionic form) and its conjugates expressed as haloxyfop-R. In line with the proposal for food of plant origin a non isomer-selective definition as sum of haloxyfop *(R,S)* (including anionic form) and its conjugates expressed as haloxyfop *(R,S)* may be considered as an option, that meets also the capability of the analytical method proposed for monitoring purposes. Again, it is noted that the proposal haloxyfop *(R,S)* does not necessarily refer to a ratio 1:1 of the two isomers.

Livestock feeding studies were conducted in lactating cows, beef cattle and laying hens. As in the livestock metabolism studies the test material was haloxyfop administered at different dose levels to the animals.
Residues in milk of lactating cows were low at all dose levels. The residues in cream were considerably higher than in milk with a highest value of 0.35 mg/kg in average at the highest dosing level that corresponds to *ca* 6 times the estimated dietary burden for dairy cattle from the representative uses evaluated. After 3-7 days of withdrawal no residues were detected (<0.01 mg/kg) in milk and cream.
In a feeding study with calves the lowest residues were found in muscle followed by fat, liver and kidney. Residues found at a dose level comparable to the estimated dietary burden for cattle (*ca* 0.5 mg/kg DM) give rise to significant residues in food of animal origin in practice and thus MRLs were propose.
In the study with laying hens residues were low in eggs and a plateau was reached at 8-10 days. Low residues were also found in muscle, while residue in liver and fat were *ca* 5 to 10 times higher than in eggs and muscle tissue. Based on the worst case estimated dietary burden for poultry and by extrapolation from the feeding study, the RMS proposed MRLs for poultry products.
It is noted that the assessment of the dietary intake of livestock including the derivation of MRLs for food of animal origin presented above is included in the addendum of July 2005 (after EPCO 24) which was however not peer reviewed.

3.3. CONSUMER RISK ASSESSMENT

The chronic dietary risk assessment for consumers is based on information obtained from supervised residue trials, feeding studies and on European and international consumption data.

The theoretical maximum daily intake (TMDI) for an adult based on the WHO model (GEMS/Food European diet) was about 52% of the proposed ADI. National Estimates of Daily Intake (NEDI) were calculated for UK consumers with the UK Rees/Day model (Two highest 97.5th percentile intakes plus mean intakes from other food). Total intakes for adults were below the ADI of 0.00065 mg/kg bw/day, accounting for ca 34% of the proposed ADI. For toddlers and infants however the total estimated intake amounts to 138% and 215% of the proposed ADI, respectively. A refined assessment, including STMR values instead of MRLs, indicated the long-term exposure being significantly below the ADI (11-18%) for all considered consumer groups.

The acute dietary risk assessment showed that the National estimated Short Term Intake (NESTI), using the UK model for adults and toddlers, is well below (10 %) the ARfD of 0.075 mg/kg bw/day in the most critical case (infants consuming carrots).

The dietary risk assessment performed for different consumer groups indicates that there are no chronic and acute concerns related to dietary exposure resulting from the representative uses.
However consumer intake of residues from groundwater used as drinking water was not considered. A high potential for ground water contamination by the metabolites DE-535 pyridinol and DE-535 pyridinone was identified. Pending submission of a new FOCUS ground water modeling in the section of fate and behaviour (refer to point 4.2.2) consumer exposure and consumer risk to these metabolites may need to be assessed.

3.4. PROPOSED MRLS

Carrot, rape seed, Soybean (seed), dry peas (pulses)	0.1 mg/kg
Kidney; poultry liver	0.05 mg/kg
Poultry fat	0.03 mg/kg
Liver other than poultry liver	0.02 mg/kg
Meat; fat other than poultry fat	0.01* mg/kg
Eggs, milk	0.01* mg/kg

It is noted that according to current legislation a lower LOQ would be required for raw commodities which are used for baby food (e.g. carrots) and infant formulae/ follow-on formulae (e.g. soya) than the LOQ considered within the peer review procedure of haloxyfop. Basically haloxyfop shall not be used in agricultural products intended for the production of this kind of food. Haloxyfop is not considered to be used if the residues do not exceed a level of 0.003 mg/kg. Therefore the notifier has been asked to develop methods that are able to analyse both raw commodities and infant follow-on

formulae for residues down to 0.003 mg/kg. A validated method for haloxyfop available to determine residues down to 0.003 mg/kg has been submitted. Also an ILV report has been submitted and was evaluated in an addendum (September 2005 – not peer reviewed).

4. Environmental fate and behaviour

Haloxyfop-R methyl ester was discussed at the EPCO experts' meeting on environmental fate and behaviour (EPCO 21) in April 2005.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Laboratory metabolism of haloxyfop-R methyl ester (DE-535) under dark aerobic conditions at 20 ºC was investigated in two studies with the active substance either ^{14}C-labelled in the phenyl or in the pyridine ring of the molecule. The six soils covered a range of pH (6.4 – 8.3), clay contents (6 – 48%) and organic matter contents (1.2 – 6.3%). One of the soils (sandy loam) was also tested at 10ºC with the pyridine-labelled compound, and one soil was sterilised and tested with the phenyl-labelled compound. Additionally, the aerobic degradation rate was investigated in three horizons of the same Borstel, German soil used for a previous lysimeter study.

The mineralization at 20 ºC was slower in the ^{14}C-pyridinol labelling soils (1.0-3.3 % AR after 90 days in four soils and 6.2-6.3% AR after 91 days in two soils) than in the^{14}C-phenyl labelling soil (32% AR after 90 days). The fractions of non-extractable radioactivity were 44% AR (90 d, phenyl-labelling) and 3.4-38% AR (after 90-91 d, pyridinol labelling).

The methyl ester was hydrolysed rapidly to **haloxyfop-R[10] (DE-535 acid)** in all six soils with only 1.3-7.7% AR remaining ester 1-2 days after treatment, when maximum levels of the acid (53-91% AR) were observed. The acid was further degraded to **DE-535 pyridinol[11],** to **DE-535 phenol[12],** and to **DE-535 pyridinone[13]**. DE-535 pyridinol exceeded the trigger value of 10% AR in all six pyridinol labelling soils, (max. 29-52% AR, after 59-91 days) but was not identified in the phenyl labelling soil. DE-535 pyridinone exceeded 10% AR on a limited number of occasions in laboratory studies (max. 11.0% AR after 120 days at 20ºC and max. 11.5% AR after 268 days at 10ºC) and DE-535 phenol reached a maximum of 12.6% AR at 14 d in a loamy clay soil and 11.6% AR at 3 d in a sandy clayey loam soil. The need to consider pyridinol, pyridinone and phenol metabolites with regard to the residue definition and potential groundwater contamination was seen during the evaluation meeting (September 2004). The applicant presented in an addendum (April 2005) some arguments to address this issue. The experts meeting (EPCO 21) concluded that even if metabolites exceed the trigger value of 10% AR only occasionally, DE-535 pyridinone and DE-535 phenol should be considered as relevant soil metabolites and they should be considered with regard to possible leaching to groundwater (see section 4.2.2).

[10] (R)-2-[4-((3-Chloro-5-(trifluoromethyl)-2-pyridinyl)oxy]phenoxy)propanoic acid
[11] 3-chloro-5-trifluoromethylpyridin-2-ol
[12] 4-(3-chloro-5-trifluoromethyl-2-pyridyloxyphenol
[13] 3-chloro-1-methyl-5-(trifluoromethyl)-2(1H)-pyridinone

Further investigations were performed on the radioactivity remaining unextracted form the soil. The results suggested typically that a greater proportion of applied radioactivity was associated with fulvic and humic acids at the earlier sampling intervals compared to the later sampling interval where increased amounts were associated with the humin.

In the sterile soil, mineralisation was less than 1% AR in 4 months. Like in the non-sterile soil degradation, haloxyfop-R methyl ester degraded rapidly to produce the acid metabolite haloxyfop-R, which reached a maximum amount of 85% AR after 30 days. No other major metabolites were identified under these conditions.

Degradation of ^{14}C-DE-535 (phenyl and pyridine labelled) under dark anaerobic conditions at 20 ºC was investigated in a study with a sandy loam soil (Marcham; pH = 7.6, 15% clay, 1.9% OM). The anaerobic degradation of ^{14}C-DE-535 pyridinol[14], ^{14}C-DE-535 phenol and ^{14}C-DE-535 pyridinone were also investigated by direct application to the separate systems of the same soil type to determine the degradation kinetics of these metabolites. The ester was hydrolysed very rapidly to DE-535 acid (maximum concentration 89% AR at 3 d). DE-535 acid once formed decreased corresponding to an increase of soil bound residues and the amount of phenol and pyridinol metabolites formed did not exceeded 1% AR.

According to the available study, photolysis does not contribute to the dissipation of DE-535 and DE-535 acid. Haloxyfop-R methyl ester was hydrolysed to form haloxyfop-R in both irradiated samples and dark controls, indicating non-photolitic conversion on the soil surfaces. No other products were formed in significant concentrations in either irradiated or dark systems, although small (max. 9.1% AR in dark controls after 5 days) and variable amounts of DE-535 phenol were formed.

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

Degradation rate of haloxyfop-R methyl ester in soil under aerobic conditions was investigated in the same soils used in the route study. DT_{50} and DT_{90} values for haloxyfop-R methyl ester and all four major metabolites were calculated for biologic active surface soils at 20ºC excluding results from deeper soil layers (Borstel soils), sterile conditions and lower temperature. In the first study both simple first order one and two compartment decay curves with accumulation phases were considered for all compounds, whilst in the second study simple first order models were used except for DE-535 acid and DE-535 phenol where bi-exponential models were used. Haloxyfop-R methyl ester is very low persistent, with DT_{50} <0.6 day (n= 7) and DT_{90} <1.8 day (n= 7). DT_{50} values for haloxyfop-R were in the range 4.0 - 13 days and DT_{90} were in the range of 31-332 days. For phenol the DT_{50} range was 15 - 110 days, with the regulatory limit value of 60 days exceeded in 2 out of 6 samples. DE-535 pyridinol and DE-535 pyridinone showed to be persistent with all DT_{50} values higher than 60 days (DT_{50} = 79–437 days and 205-246 days, respectively) and most of the DT_{90} values higher than 1 year.

The rate of degradation of ^{14}C-haloxyfop-R methyl ester (phenyl and pyridine labelled) under anaerobic conditions was < 2 days. Haloxyfop-R, DE-535 phenol and DE-535 pyridinone

[14] The original Table B.8.1.1.2.1/01-2 included the DAR has been revised regarding results for DE-535 pyridinol (addendum dated April 2005).

metabolites, once formed, degraded slowly, with DT_{50} values of 588 days, 281 days, and 306 days, respectively.

Dissipation of haloxyfop-R and DE-535- pyridinol in soil under field conditions was investigated through 18 months in two sites in France and two sites in Germany, which were applied with haloxyfop-R methyl ester formulated as EF-1400 (108 g a.s./ha on bare soil) in late spring/early summer months. A second study was carried out with the same compound following autumn application to three sites in Germany. No concentration profiles were measured for haloxyfop-R methyl ester, DE-535 phenol and DE-535 pyridinone. Residues of both haloxyfop-R and DE-535-pyridinol were found primarily in the top 10 cm of the soil column. DT_{50} values for haloxyfop-R were in the range of 5-27 days and DT_{90} in the range 53-362 days. Concerns were raised on the degradation rates calculated for DE-535 pyridinol in the first study (spring/summer application) as they were based on few experimental measurements and because of the variability of data obtained in three out of four field experiments (Bas-Rhin (France), Baden-Wurtemberg (Germany) and Champagne (France) soils). In addition, the DT_{50} value of 153 days, calculated in the second study (autumn application) for the Schenkenberg (Germany) soil, resulted in a poor goodness of fit (r^2 = 0.42). The acceptability of these $DT_{50field}$ values was not fully discussed at the meeting of experts, but it is the opinion of EFSA and the rapporteur Member State that they should not be considered for the risk assessment. However, as PECsoil calculations for DE-535 pyridinol were performed with the longest field DT_{50} value of 193 days derived from the Klostergut (D) soil, the exclusion of the above mentioned data will not have an impact on the final assessment. Reliable field DT_{50} values for DE-535 pyridinol were in the range of 38-193 days and DT_{90} in the range of 412-640 days. As some of the $DT_{50field}$ values and all the $DT_{90field}$ values exceeded the regulatory limit values, pyridinol can be considered a persistent major metabolite.
The accumulation potential of haloxyfop-R methyl ester and its metabolites (acid and pyridinol) in soil under field conditions was investigated over a five-year period under typical use conditions in Germany and France (single annual application to bare soil of nominally 108 g a.s./ha of DE-535 formulated as EF-1400). All quantifiable concentrations (LOQ = 2.0 µg/kg) were found in the top 0-10 cm. The maximum concentrations of DE-535 acid were 73.2 µg/kg in Germany (immediately after treatment 2) and 59.5 µg/kg in France (immediately after treatment 3). DE-535 pyridinol levels reached a maximum of 3.6 µg/kg. In conclusion, there was no evidence of any accumulation of the two metabolites DE-535 acid and DE-535 pyridinol in soil. DE-535 phenol and DE-535 pyridinone were not analysed.

In the original DAR, PECsoil values for haloxyfop-R methyl ester and its major metabolites were calculated based on worst case laboratory DT_{50} values. The meeting of experts (EPCO 21) agreed on the use of the realistic worst case DT_{50} from the field dissipation studies where available (i.e. haloxyfop-R and DE-535 pyridinol). New PECsoil calculations for haloxyfop-R and DE-535 pyridinol were provided in an addendum dated April 2006 (not peer reviewed). However, after the EPCO meeting, the EFSA noted that the method (bi-exponential degradation model) used to determine degradation rates for all the metabolites were not consistent with the method assumed by

the model for PECsoil calculations (first order). As a consequence, the rapporteur Member State agreed with the EFSA that new calculations should be performed for haloxyfop-R, DE-535 phenol and DE-535 pyridinone[15]. However, it should be noted that new PECsoil values will not have an impact on the risk assessment for terrestrial organisms as safe use have been shown using the initial PECsoil values.

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

Sorption characteristics of the primary metabolite haloxyfop-R were investigated in one standard soil and three agricultural soils. In another study sorption characteristics for the metabolite haloxyfop-R was studied on four different soils, one of which constituted three horizons of soil from a lysimeter, and metabolites DE-535 pyridinol, DE-535 phenol and DE-535 pyridinone were investigated in seven different European soils. Only one concentration of the substance was used and no Freundlich isotherms were derived. Sorption coefficients for haloxyfop-R methyl ester were not determined due to rapid hydrolysis. Haloxyfop-R was weakly adsorbed to soil, with a K_{OC} in the range from 29 to 114 mL/g (mean = 53.5 mL/g), indicating that this metabolite is high to very high mobile in soil. In deeper soils (from 30 cm to 100 cm) K_{OC} values for haloxyfop-R were in the same range (55-60 mL/g). DE-535 pyridinol and DE-535 pyridinone were even more weakly adsorbed with K_{OC} ranging from 23.4 to 67.8 mL/g (mean= 41.9 mL/g) and from 18.5 to 46.3 mL/g (mean= 30.8 mL/g) respectively. However, results for DE-535 phenol indicate that this major metabolite is low mobile in soil (K_{OC} = 657.8 – 967.6 mL/g, mean = 761.5 mL/g).

The behaviour of haloxyfop-R methyl ester was studied in 3 lysimeter studies representing three application seasons under typical conditions for Northern Europe (Germany). The lysimeters were undisturbed soil monoliths of sandy soils sown with sugar beet (2 lysimeters) or oil seed rape and treated on late spring (middle of June) or early spring (middle of May) for sugar beet or autumn (late September) for oil seed rape. Labelled haloxyfop-R methyl ester at rates equivalent to 52.7 – 112 g a.s./ha (approximately minimum and maximum label application rates) was used. In the late spring study, one lysimeter was treated at rate equivalent to 212 g a.s./ha. Leachates were collected throughout the two-year period experiments and analysed for the total radioactivity. Leachate was analysed for haloxyfop-R methyl ester and the haloxyfop-R, DE-535 phenol (only 2 studies) and DE-535 pyridinol metabolites. No measurements were made for DE-535 pyridinone. Haloxyfop-R methyl ester itself was shown to disappear rapidly from the soil columns and was never detected in the leachates. Concentrations of DE-535 phenol in leachate were < 0.004 µg a.s. eq/L. DE-535 pyridinol was found not to exceed 0.1 µg a.s. eq/L in any leachate sample. Haloxyfop-R exceeded 0.1 µg a.s. eq/L in some leachate samples, but the annual average concentrations were in the range from <0.004 µg a.s. eq/L to 0.089 µg a.s. eq/L. An uncharacterized polar component (U1) in the leachate samples was found at annual average concentrations > 0.1 µg a.s. eq/L in the early spring application study

[15] In the case of DE-535 pyridinol, the $DT_{50field}$ used for PECsoil calculations was obtained with a three-exponential function. However, as this half-life approximates a 1st order kinetic (DT_{50} = 193 d, DT_{90} = 640 d), it is the opinion of EFSA that no new calculations for this metabolite are required.

and in the autumn application study. The 90% of U1 was identified as trifluoroacetic acid (TFA). The highest annual average concentrations measured were 0.085 µg/L in the spring study and 0.079 µg/L in the autumn study. The meeting of experts (EPCO 21) agreed that, as the trigger value of 0.1 µg/L was not reached, no further assessment (i.e. groundwater modelling) was necessary for trifluoroacetic acid.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

The hydrolysis of haloxyfop-R methyl ester was investigated in natural water (pH 8) and buffered (pH 4, 7 and 9) sterile water in the dark with both pyridine and phenyl ring radiolabelled compound. The hydrolysis rate was found to be strongly correlated with increasing pH: calculated half-lives at 20 ºC ranged from 0.63 days (pH 9) to 43 days (pH 7); while at pH 4 the material was stable. Degradates analysis showed that in natural water and pH 7 and pH 9 buffers, haloxyfop-R methyl ester hydrolysed to haloxyfop-R (max. 99.1% AR after 21 days at pH 9). Two degradates were seen in both label forms. They reached maximum concentrations of 2.3% AR and 2.9% AR for pH 9 and pH 7, respectively.

Photolysis of haloxyfop-R methyl ester (labelled at the pyridine or at the phenyl ring) was investigated in pH 5 sterile buffer and natural water (pH 8.5) with a xenon light source for up to 20 days. In sterile buffer haloxyfop-R methyl ester degraded in the irradiated samples to form two major metabolites: an isomer of DE-535 pyridinol (max. 14.3% AR) and **DE-535 furan** (max. 18.6 % AR after 6.8 days of continuous irradiation). Very little degradation took place in dark controls. Photodegradation of haloxyfop-R methyl ester in natural water resulted in rapid production of haloxyfop-R (max. 99% AR) via hydrolysis in both irradiated and dark control samples. In irradiated systems, two additional metabolites exceeding 10% AR were produced: **4-trifluoromethyl-5-amino-pentanol** (**DE-535 TAP**, maximum 17.8 % AR) and DE-535 pyridinol isomer (maximum 16.2 %AR). In pH 8.5 natural water system, DE-535 furan attained a maximum of 6.8% AR after 1.8 days. Concerns were raised on the potential relevance of the metabolite DE-535 furan formed in the sterile buffer system, because of the dibenzofuran “like” structure of this metabolite. The experts of the environmental fate and behaviour section (EPCO 21) addressed this issue to the experts of the ecotoxicolgy section (EPCO 22) and of the mammalian toxicology section (EPCO 23). The applicant provided some risk-based arguments in an addendum on April 2006 (not peer reviewed). A PEC_{sw} value of 0.4 µg/L for DE-535 furan was calculated based on a combined spray drift and drain flow/runoff peak PEC_{sw} of haloxyfop-R methyl ester, and the assumption of a maximum formation fraction of 7% for DE-535 furan from the parent. This calculation can be considered as a preliminary estimation for TER calculation. However, since a clear conclusion on the ecotoxicological and toxicological relevance cannot be drawn (see sections 2.8 and 5.2), it is the opinion of EFSA that DE-535 furan needs to be addressed with respect of surface water compartment.

The photodegradation of haloxyfop-R in sterile buffer was also investigated. The photoproduct profile was similar to that observed for haloxyfop-R methyl ester in natural water, although DE-535

phenol (max. 26.0% AR after 8.8 days) and **DE-535 acid phenone** (max. 22.2% AR after 6.8 days) were observed as significant photoproducts. DE-535 pyridonol isomer reached a maximum level of 11.6% AR after 6.8 days).
The net photolysis first order half-lives was of 2 days in natural water and 20 days in pH 5 buffer for haloxyfop-R methyl ester and 8 days (in natural water) 12 days (in pH 5 buffer) for haloxyfop-R (comparable to natural sunlight intensity in the summer season at 40º N latitude). It may be concluded that photolysis may contribute to the environmental degradation of haloxyfop-R methyl ester and haloxyfop-R.

Haloxyfop-R methyl ester was shown not to be readily biodegradable in a 28-day closed bottle test.

The degradation of haloxyfop-R methyl ester was investigated in two natural water-sediment systems (one low organic sandy system and one high organic silt loam system) under controlled laboratory conditions with (^{14}C-phenyl)- and (^{14}C-pyridine)-labelled material. The total radioactivity in surface water ranged from 80-85% AR (high organic system) and 74-87% AR (low organic system) at 0 time to 8-32% AR and 6-31% AR at study end (100 days). Levels of %AR in sediment extracts were higher in the high organic silty loam sediment (max. 36-43% AR) than in the low organic sandy sediment (max. 20-23% AR). At the end of the study (100 days) the total amount of non-extractable residue was in the range 22 – 27% AR. Carbon dioxide production reached a maximum value of 49-53% AR at 100 days. The following identified breakdown products accounted for > 10% AR: DE-535 acid (max. 63.8-81.5 %AR in water, max. 12.7-33.7 % AR in sediment) and DE-535 pyridinol (max. 19.7 %AR in water, max. 16.4 %AR in sediment, both detected only with the ^{14}C-pyridine-labelled material). Lower levels (max 5.2% AR) of the DE-535 phenol were detected. Calculated first order DT_{50} values for haloxyfop-R methyl ester were < 0.3 days. First order DT_{50} values for haloxyfop-R were 39-52 days (whole system), 32-55 days in the water phase, whereas degradation in the sediment phase was slow in the low organic sandy system (> 1 year). Degradation rate constants calculated in the DAR for DE-535 pyridinol were considered not reliable, since the percentage of the metabolite increased until the end of the study. The experts in EPCO 21 agreed that a water/sediment study with a longer duration is not deemed appropriate. However, as the precursors of DE-535 pyridinol were still present in the system at study termination, it was concluded that surface water exposure assessment should be performed with a worst case assumption based on formation fraction of the metabolite and precursors.
Actual and time weighted average surface water and sediment concentrations for haloxyfop-R methyl ester, haloxyfop-R and DE-535 pyridinol were recalculated by the rapporteur Member State assuming a water volume with a depth of 0.3 m and distance of 1 m from the source (with an input from spray drift of 2.77% of the application rate). Additional calculations were performed including a contribution from run-off/erosion and/or drainage flow of 15% of the application rate which occurs on the day of application (in accordance with guidelines provided in the EC Guidance Document on Aquatic Ecotoxicology Sanco 3268/2001 ver. 4). Compared to the FOCUS step 1 assumption of 10%, this approach was accepted and considered an absolute worst case by the meeting of experts, and the final calculation and decision could be taken at Member State level. New PEC_{sw} and PEC_{sed}

calculations for DE-535 pyridinol were performed and included in addendum 2 of April 2006. It was assumed that DE-535 pyridinol's potential precursors (DE-535 acid and DE-535 phenol) are converted completely to DE-535 pyridinol. The resulting conversion factor was 56.24%, based on the concentration of DE-535 pyridinol (33.13%) plus the concentrations of the precursors haloxyfop-R (17.85%) and DE-535 phenol (5.26%). Assuming complete conversion of DE-535 pyridinol's precursors, PEC_{sw} values were increased by a factor of 1.7. In addition PEC_{sed} values were recalculated taking into account a sediment bulk density of 1.3 g/m^3, in place of 1.5 g/m^3 as originally done in the DAR. Results have not been peers reviewed but the rapporteur Member State and the EFSA considered the study acceptable.

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

The leaching to groundwater of haloxyfop-R, DE-535 pyridinol, DE-535 phenol, and DE-535 pyridinone was modelled for the nine European FOCUS scenarios using FOCUS PELMO 2.2.2. To represent worst case scenarios for the soil degradates, they were modelled as "applications" at their corresponding maximum amounts seen in the laboratory experiments, corrected for molecular weight. Degradation rates for all compounds were derived from laboratory studies and resulted in average DT_{50lab} values (corrected for moisture contents) of 11.4 d, 230 d, 36.1 d and 226 d for haloxyfop-R, DE-535 pyridinol, DE-535 phenol, and DE-535 pyridinone respectively. All applications were modelled to the crop (autumn/late autumn application to winter oilseed rape and spring/early spring application to sugar beet) to represent post-emergence application. The 80th percentile annual average haloxyfop-R concentrations in the leachate at 1 m depth were estimated to be below 0.1 µg/L. The major metabolite DE-535 pyridinol exceeded the limit value of 0.1 µg/L in all scenarios, with 80th percentile annual average PEC_{gw} in the range of 0.55-2.87 µg/L. DE-535 pyridinone also exceeded the trigger value for groundwater in all scenarios (PEC_{gw} ranged from 0.26 to 0.90 µg/L). DE-535 phenol were in all cases < 0.001 µg/L. The mobility of DE-535 has not been modelled due to fast degradation (hydrolysis) in soil (DT_{50} < 0.7 d) and it is therefore not expected to be present in groundwater. The reliability of new higher tier PEC_{gw} modelling study (including the metabolite TFA found in the lysimeter studies) submitted by the applicant and summarised in an addendum (April 2005) was discussed at the experts' meeting. Some of the assumptions used in the modelling (constant degradation assumed in the top 1 m horizon for DE-535 pyridinol; a 1% formation factor derived from lysimeter studies and the extrapolated DT_{50}field for DE-535 pyridinone) were not accepted and therefore it was concluded that the risk assessment should be based on the original calculations reported in the DAR. However, during the preparation of the conclusion, EFSA noted that the methods used to determine degradation rates from the experimental data for all the compounds (bi-phasic degradation model or three exponential function) were not compatible with the method assumed by the PELMO model (first order kinetic). Therefore, it was agreed with the rapporteur Member State that these values should be taken with caution and new FOCUS groundwater modelling should be performed taking into account the recommendations of the FOCUS group. Pending the outcome of the new FOCUS modelling for groundwater, an evaluation of the relevance of the metabolites following the guidance document on relevant metabolites

(SANCO/221/2000) has to be completed. In the case the trigger of 0.1 µg/L or 0.75 µg/L is exceeded there is a need to provide information on the toxicological properties and possibly consumer risk assessment.

Following a data gap identified at the meeting of experts, the applicant provided[16] some explanations on the differences between the concentrations of haloxyfop-R resulting from the groundwater modelling and the lysimeter studies.

4.3. FATE AND BEHAVIOUR IN AIR

The volatilisation of DE-535 from soil and plant surfaces was investigated in one study. Results of the plant tests showed that 19 and 20% AR had volatilised from the plant leaves after 24 hours. Losses from soil were much lower at only 2% AR. The potential for photochemical degradation of DE-535 in air is high (DT_{50}= 0.62 days estimated with the Atmospheric Oxidation Program), indicating low po

5. Ecotoxicology

Haloxyfop-R was discussed at the EPCO experts' meeting for ecotoxicology (EPCO 22) 11-15 April 2005.

5.1. RISK TO TERRESTRIAL VERTEBRATES

Acute toxicity tests with birds using haloxyfop-R-methyl ester (DE-535) and the metabolite DE-535 acid are available. Short-term dietary and reproduction toxicity tests were conducted only with the acid metabolite. This was considered sufficient by the MS experts since the haloxyfop-R-methyl ester rapidly degrades to the acid in plants and hence birds are unlikely to be exposed to the ester. The DE-535 acid was more acutely toxic to birds than the methyl ester in comparable studies. No bird toxicity study with the lead formulation is available. It was the opinion of the meeting that this should not be required for reasons of animal welfare and was not considered necessary since the formulation has a high content of the active substance.

A first tier risk to birds using generic species representing small insectivorous and large herbivorous birds in the short grass scenario was performed in accordance with SANCO/4145/2000 in the DAR. The assessment was complemented with a medium herbivorous bird in the leafy crop scenario in addendum 1 of April 2005. All TER values are above the relevant Annex VI trigger indicating a low risk to birds from the evaluated representative uses. It was however noted that the DT_{50} in treated vegetation was longer than the default value of 10 days. The MS experts therefore agreed that the f_{TWA} values should to be revised for each crop and consequently also the risk assessment. Crop specific residue decline data for sugar beet, field beans, field peas and oilseed rape were presented in addendum 2 of April 2006 (not peer reviewed) based on studies already included in section B.7.6 of

[16] Comments from the applicant are included in the evaluation table and accepted by the rapporteur Member State (data gap 4.2). The data gap is not relevant for the final risk assessment.

the DAR. Resulting DT_{50} values were in the range 7.2 – 31.6 days based on a first order kinetic model. It should however be noted that the number of data points in the residue studies are few, and no initial concentrations were analysed. It is the view of the EFSA that DT_{50} values in vegetation are not well founded. However, if the longest DT_{50} of 31.6 days that was estimated for sugar beet is used to calculate the f_{twa} and the subsequent TER for herbivorous birds, a TER_{lt} value above the trigger would still be the result.

The first tier risk assessment for mammals was done in accordance with SANCO/4145/2000 using values for medium herbivorous and insectivorous mammals. The acute TERs were 114 and 315 respectively, and hence well above the Annex VI trigger of 10. The long-term TERs were 0.05 and 0.086, respectively, and hence significantly below the Annex trigger of 5 indicating a high risk.

The initial long-term risk assessment in the DAR was based on a NOEL of 0.03 mg/kg bw/day for minor changes in haematology and clinical chemistry observed in a two-year dietary chronic toxicity-oncogenicity study. The rapporteur Member State proposed to refine the assessment of long-term risk to mammals by choosing the NOAEL of 2 mg a.s./kg bw/day from a 16-week dietary study with rats. Additionally, a mean 21-day residue level based on mean DT_{50} and average of residues in four different crops was used. The refinements were discussed by the MS experts and it was agreed that a NOAEL of 1 mg a.s./kg bw/day from the reproduction study should be used. The NOAEL/NOEL chosen for reproductive effects in the mammalian toxicology section was set to 0.065 mg/kg bw/day based on decreased body weight of the pups after 21 days at 1.0 mg/kg bw/day. As for birds, it was also considered necessary to recalculate the f_{TWA} values for each crop and a revise the risk assessment based on the new values. Since a TER of 2.9 is obtained for insectivorous mammals if a NOAEL of 1 mg/kg bw/day is used, and TER values below the Annex trigger of 5 are likely to be the result for herbivorous mammals, the long-term risk to mammals needs to be further addressed. The EFSA proposes that the PPR Panel opinion on the choice of endpoint to assess the long-term risk to mammals is considered in this assessment[17].

The $logP_{ow}$ for haloxyfop-R-methyl ester is 4.0. However, since the methyl ester degrades rapidly to the acid in both soil and water, the potential for bioaccumulation and food chain transfer is considered as low. The BCF for the metabolite DE-535 acid was determined to 17.0, and therefore the risk for secondary poisoning of birds and mammals is considered to be low.

No assessment of the risk to birds and mammals from intake of contaminated drinking water is available. This issue needs to be addressed before a final conclusion can be drawn.

[17] Opinion of the Scientific Panel on Plant health, Plant protection products and their Residues on a request from the EFSA related to the choice of endpoints to assess the long term risk to mammals, The EFSA Journal(2006) 344, 1-22. http://www.efsa.eu.int/science/ppr/ppr_opinions/1437/ppr_op_ej344_noec_mammals_en1.pdf

5.2. RISK TO AQUATIC ORGANISMS

Based on the available acute toxicity data, haloxyfop-R methyl ester is classified as very toxic to aquatic organisms with a LC_{50} of 0.0884 mg/L for bluegill sunfish (*Lepomis macrochirus*), the most sensitive species tested. Studies using rainbow trout (*Oncorhynchus mykiss*) with the ester and the acid forms show that the ester form is more acutely toxic to fish than the acid. LC_{50} values were >50 mg/L and 0.46 mg/L for the acid and ester respectively. Also for species representing aquatic invertebrates, algae and macrophytes the acid form appears to be less toxic or of similar toxicity compared to the ester form. Studies with all four groups of aquatic organisms are also available with the metabolite DE-535 pyridinol. The formulation was not more toxic than expected based on the content of the active substance.

For the intended uses first tier TER values were calculated by comparing the toxicity endpoints from the most sensitive species with PEC_{sw} calculated from spray drift at 1 m distance from the treated crop to a 30 cm deep static water body. Additionally, TER values were calculated assuming contribution from drainage and runoff events corresponding to 15% of the application rate. The 15% contribution was seen as a worst case. The acute TER value for haloxyfop-R methyl ester obtained for fish is 89 (based on spray-drift) or 16 (based on drainage/runoff alone). The long-term TER for fish is 43 (spray drift) or 6.7 (spray drift + drainage/runoff) based on maximum PEC_{sw}. All other TER values for haloxyfop-R methyl ester, the metabolites DE-535 acid and DE-535 pyridinol are well above the relevant Annex VI trigger for all groups of aquatic organisms. Risk mitigation measures corresponding to 5 m buffer zones are required to protect fish from exposure via spray drift. The rapporteur Member State argued that the contribution from drainage/runoff in reality could be expected to be much lower than 15% since haloxyfop-R methyl ester degrades very fast in soil.

The Member State experts discussed the long-term risk assessment for fish and the rapporteur Member State was asked to verify the choice of the endpoint. The true NOEC for rainbow trout in the 28-day flow through study was 0.0052 mg/L. The rapporteur Member State chose 0.0427 mg/L since at this concentration mild toxic effects were observed first on day 3 and the number of fish with symptoms decreased after day 16 indicating reversibility of the effects. The TER_{lt} was calculated to 464 based on a 28-day TWA PEC_{sw}. If a 28-d TWA PEC is applied, which could be reasonable considering the rapid dissipation of haloxyfop-R methyl ester from surface water and low toxicity of the metabolites, a TER_{lt} above the Annex VI trigger would be obtained even using the NOEC of 0.0052 mg/L and a PEC based on spray drift + 15% drainage/runoff at a distance of 1 m from the field (TER=57; calculation not included in the DAR or addendum).

The metabolite DE-535 furan was found in a photolysis study using sterile water at levels >10%. In a photolysis study using natural river water the level of the metabolite was 6.8% of the applied amount. The metabolite was discussed in the expert's meeting and it was agreed that the applicant should address the toxicological relevance of the furan. In addendum 2 of April 2006 (not peer reviewed) a risk assessment based on the assumption of a formation fraction of 7%, a PEC_{sw} of 6.4 µg/L for haloxyfop-R methyl ester from a combined spray drift and drainage/runoff contamination, and equal

toxicity as the parent was presented. The resulting TER would be above the Annex VI trigger. However, if an assumption of ten times higher toxicity is done; the TER would be below the trigger. Since no information on the toxicity of the DE-535 furan has been presented a clear conclusion cannot be drawn and therefore additional data is required.

Haloxyfop-R methyl ester was detected at >10% of applied radioactivity in the sediment within the first day of the water/sediment study but then decreased to <10%. Since the NOEC for haloxyfop-R-methyl and the metabolite DE-535 acid are >0.1 mg/L for *Daphnia magna* no study to assess the risk to sediment dwelling organism is required. However, a 28-day study with *Chironomus riparius* is available. This study also covers the acid metabolite due to rapid degradation of the methyl ester in water. The TER value, calculated with a PEC_{sw} based on spray drift at 1 m and 15% drainage/runoff, is 391 indicating a low risk. No study with *Chironomus* is available for the metabolite DE-535 pyridinol. Since this metabolite is persistent in sediment it was agreed by the MS experts that such a study should be required.

Since haloxyfop-R-methyl ester dissipates very fast from the water phase and is of low persistence in the sediment the potential for bioaccumulation is low. The bioconcentration factor for DE-535 acid was determined to 17.0 and hence the potential for bioaccumulation in the food chain also from the metabolite is considered as low.

The metabolites DE-535 pyridinol and DE-535 pyridinone were found in concentrations >0.1 µg/L in the FOCUS ground water modelling. Acute toxicity studies with fish, daphnids, algae and aquatic plants using DE-535 pyridinol were included in the DAR. The risk assessment was included in addendum 2 of April 2006 and has not been peer reviewed. However, the EFSA can agree to that the risk to aquatic organisms from this metabolite is low. Regarding the metabolite DE-535 pyridinone, studies on all groups of aquatic organisms have been submitted recently but are not evaluated by the rapporteur Member State.

5.3. RISK TO BEES

Toxicity to bees was tested with haloxyfop-R methyl ester, the DE-535 acid and the lead formulation. The study using the ester was not fully accepted. However, a low toxicity was indicated with all three test materials. The oral and contact HQ quotients are 1.1 and 1.9 respectively, based on content of haloxyfop-R methyl ester in the formulation. For DE-535 acid, the HQ value is 1.1 for both oral and contact exposure. Since all HQ values are clearly below the Annex VI trigger of 50 a low risk to bees was concluded.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Non-target arthropods may be exposed to haloxyfop-R methyl ester by direct over spraying and/or by contact with residues on vegetation or soil. All tests with non-target arthropods were performed with the formulated product EF-1400. Effects on mortality of 91% and 100% were observed in glass plate tests with the indicator species *Aphidius rhopalosiphi* and *Typhlodromus pyri* at the recommended

dose rate. Effects were <30% for both species in extended laboratory tests with natural plant substrate. Studies are also available with *Poecilius cupreus, Chrysoperla carnea, Episyrphus balteatus* and *Aleochara bilineata*. For all species except *C. carnea* effects on mortality and fecundity were <30%. For *C. carnea* the effect on mortality was 16% while fecundity was increased with 75%. The risk to non-target arthropods is considered to be low.

5.5. RISK TO EARTHWORMS

Acute toxicity studies with earthworms are available for haloxyfop-R methyl ester, DE-535 acid and with the formulated product EF-1400. The formulated product was more toxic than expected based on the content of haloxyfop-R methyl ester. In the original assessment no correction of the end point values for a log P_{ow} >2 had been done. New corrected values and a subsequent risk assessment are presented in addendum 2 of April 2006 (not peer reviewed). However, the values from the studies with the formulation had not been corrected. All acute TER values are well above the Annex VI trigger of 10, also for the formulation, indicating a low risk. A long-term/reproduction study with the formulated product did not show any effects on mortality, growth or reproduction at a dose rate of 1.08 mg a.s./ha. Based on the uncorrected NOEC (highest concentration tested) a TER of 7.5 was obtained. If a corrected NOEC is used the TER will be below the Annex trigger of 5. However, it is the EFSA opinion that acute and long-term risk to earthworms can be considered as low. Haloxyfop-methyl ester degrades very rapidly in soil and the bioavailability of DE-535 acid is not expected to be significantly affected by the content of organic material in the soil. Additionally, the initial PEC_{soil} was used in the calculation and no indications of effects were observed in the study.

Three major metabolites with DT_{90} values longer than 1 year were detected in the aerobic soil degradation study. Acute and reproduction studies with the metabolites DE-535 pyridinol, DE-535 pyridinone and DE-535 phenol was submitted to the rapporteur Member State in February 2006, but has not been evaluated due to the late submission. The risk to earthworms from exposure to these metabolites can only be concluded once all studies have been evaluated.

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

No studies on other non-target soil macro-organisms were included in the DAR. For the soil metabolites DE-535 pyridinol, DE-535-phenol and DE-535-pyridinone the risk needs to be addressed. For these metabolites the soil DT_{90} was estimated to be longer than 1 year and hence a litterbag study is required. Litterbag studies with the formulated product EF 1499 and the metabolite DE-535 pyridinol was submitted to the rapporteur Member State in December 2005 but has not been evaluated. The risk to soil organisms can only be concluded once all studies have been evaluated.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effect on soil respiration and nitrogen transformation was tested with the formulated product. Effects after 28 days were <25% also at a dose rate above the proposed. The study is considered to cover also the effects of the metabolite haloxyfop-R since this metabolite is formed very rapidly in

soil. Studies on effects on soil micro-flora with DE-535 pyridinol and DE-535 pyridinone were submitted in January 2005 and February 2006 respectively, but have not been evaluated by the rapporteur Member State. No study with the metabolite DE-535 phenol is available. The risk to soil micro-organisms can only be concluded once all studies have been evaluated.

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

No information was available to asses the risk to non-target plants in the DAR. Data were submitted to the rapporteur Member State in March/April 2004 but has not been evaluated by the rapporteur Member State.

A summary of the assessment of pesticidal activity of the metabolites DE-535 pyridinol and DE-535 pyridinone is included in addendum 2 of April 2006. The metabolites did not show any herbicidal activity towards grass species and no insecticidal activity was observed. DE-535 pyridinol was also screened for fungal activity, with no effect observed.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

A study on activated sludge respiration rate with haloxyfop-R acid did not show any effects at 100 mg/L. The risk to biological methods of sewage treatment is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: haloxyfop-R methyl ester (DT_{90} < 3d), haloxyfop-R[18], DE-535 pyridinol[19], DE-535 pyridinone[20], DE-535 phenol[21]

Definitions for monitoring[22]: haloxyfop, its salts and esters, DE-535 pyridinol, DE-535 pyridinone, DE-535 phenol

Water

Ground water

Definitions for exposure assessment: haloxyfop-R methyl ester, haloxyfop-R, DE-535 pyridinol, DE-535 pyridinone

Definitions for monitoring[23]: haloxyfop, its salts and esters, DE-535 pyridinol, DE-535 pyridinone

[18] (*R*)-2-[4-((3-Chloro-5-(trifluoromethyl)-2-pyridinyl)oxy]phenoxy)propanoic acid
[19] 3-chloro-5-trifluoromethylpyridin-2-ol
[20] 3-chloro-1-methyl-5-(trifluoromethyl)-2(1H)-pyridinone
[21] 4-(3-chloro-5-trifluoromethyl-2-pyridyloxyphenol
[22] Preliminary residue definition pending on the outstanding data on ecotoxicological relevance of DE-535 pyridinol, DE-535 pyridinone, DE-535 phenol
[23] Preliminary residue definition pending on results of new FOCUS groundwater modelling for haloxyfop-R, DE-535 pyridinol, DE-535 pyridinone, and DE-535 phenol.

Surface water

Definitions for risk assessment: haloxyfop-R methyl ester, haloxyfop-R, DE-535 pyridinol, DE-535 furan (aqueous photolysis metabolite)

Definitions for monitoring: DE-535 furan[24] (aqueous photolysis metabolite)

Air

Definitions for risk assessment: haloxyfop-R methyl ester, haloxyfop-R

Definitions for monitoring: haloxyfop-R methyl ester, haloxyfop-R

Food of plant origin

Definitions for risk assessment: sum of haloxyfop -R methyl ester, haloxyfop-R (including anionic form) and its conjugates expressed as haloxyfop-R.

Definitions for monitoring: sum of haloxyfop -R methyl ester, haloxyfop-R (including anionic form) and its conjugates expressed as haloxyfop-R.

Optional: sum of haloxyfop (R,S) methyl ester, haloxyfop (R,S) and its conjugates expressed as haloxyfop (R,S)[25].

Food of animal origin

Definitions for risk assessment: sum of haloxyfop-R (including anionic form) and its conjugates expressed as haloxyfop-R.

Definitions for monitoring sum of haloxyfop-R (including anionic form) and its conjugates expressed as haloxyfop-R.

Optional: sum of haloxyfop (R,S) and its conjugates expressed as haloxyfop (R,S)[26].

[24] Preliminary residue definition pending on the outstanding data on ecotoxicological relevance.

[25] Does not necessarily refer to a ratio 1:1 of the two isomers.

[26] Does not necessarily refer to a ratio 1:1 of the two isomers.

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Haloxyfop-R methyl ester	very low persistent ($DT_{50\ lab}$<0.6 d; $DT_{90\ lab}$ < 3d at 20ºC and 40% MWHC)	See 5.5
Haloxyfop-R	very low to low persistent ($DT_{50\ lab}$ = 4.0-13 d, $DT_{90\ lab}$ = 31-332 d, at 20ºC and 40% MWHC)	Assessed in the DAR. Low risk has been shown.
DE-535 pyridinol	medium to high persistent ($DT_{50\ lab°}$ = 79-437 d, $DT_{90\ lab}$ = 262-1386 d, at 20ºC and 40% MWHC)	Study submitted but not evaluated. No conclusion can be drawn.
DE-535 pyridinone	high persistent ($DT_{50\ lab}$ = 205, 246 d, $DT_{90\ lab}$ = 475, 666 d, at 20ºC and 40% MWHC)	No data available
DE-535 phenol	moderate to high persistent ($DT_{50\ lab}$ = 15-110 d, $DT_{90\ lab}$ = 53->365 d, at 20ºC and 40% MWHC)	No data available

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological relevance
Haloxyfop-R methyl ester	No test due to rapid hydrolysis	FOCUS modelling: no data (not expected to reach groundwater due to rapid hydrolysis) Lysimeter: no trigger exceeded	Yes	Yes	Yes
Haloxyfop-R	high to very high mobile (K_{oc} = 28.5 – 113.5 mL/g)	FOCUS modelling: no trigger exceeded (data to be confirmed by new modelling) Lysimeter: no trigger exceeded	Yes	Yes	No assessment necessary
DE-535 pyridinol	high to very high mobile (K_{oc} = 23.4 – 67.8 mL/g)	FOCUS modelling: trigger exceeded in 9 FOCUS scenarios (0.55-2.87 µg/L) (data to be confirmed by new modelling) Lysimeter: no trigger exceeded	No	No specific studies available	Less toxic than haloxyfop-R methyl ester. The risk assessed to be low
DE-535 pyridinone	very high mobile (K_{oc} = 18.5 – 46.3 mL/g)	FOCUS modelling: trigger exceeded in 9 FOCUS scenarios (0.26-0.90 µg/L) (data to be confirmed by new modelling) Lysimeter: no data	No	No specific studies available	Studies available but not evaluated

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological relevance
DE-535 phenol	low mobile (K_{oc} = 658 – 968 mL/g)	FOCUS modelling: no trigger exceeded (data to be confirmed by new modelling) Lysimeter: no trigger exceeded	No data available	No specific studies available	No assessment necessary, pending new FOCUS calculations an assessment might be necessary

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Haloxyfop-R methyl ester	See 5.2
Haloxyfop-R	Less toxic than haloxyfop-R methyl ester to all groups of aquatic organisms tested. Risk assessed to be low.
DE-535 pyridinol	Less toxic than haloxyfop-R methyl ester to all groups of aquatic organisms tested. Risk assessed to be low.
DE-535 furan (aqueous photolysis metabolite)	No data available

Air

Compound (name and/or code)	**Toxicology**
Haloxyfop-R methyl ester	No studies available
Haloxyfop-R	No studies available

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

- A justification for using reference standards which are not the analytes for the validation of the methods for the determination of impurities in the technical material ((study announced for May, 2006; data gap identified at the meeting of experts)
- A theoretical assessment of the possible oxidising properties for haloxyfop-R methyl ester (study announced for May, 2006; data gap identified at the meeting of experts)
- Depending on the final residue definition for food of plant and animal origin, soil and water (ground and surface), it could be necessary to require enantio selective methods (refer to section 1, 3 and 6).
- Medical data is lacking. Data gap identified after the experts meeting (refer to 2.9).
- Potential surface water contamination for the aqueous photolysis metabolite DE-535 furan to be addressed, (relevant for all representative uses evaluated; data gap identified in the EPCO meeting; no submission date proposed by the applicant; refer to point 4.2)
- New FOCUS groundwater modelling in line with the recommendations of the FOCUS group about the compatibility of method used to determine degradation rates in soil from the experimental data and the method assumed by the model for degradation (relevant for all representative uses evaluated, data gap identified after the EPCO meeting, no submission date proposed by the applicant, refer to point 4.2)
- Pending the outcome of the new FOCUS modelling for groundwater, an evaluation of the relevance of the metabolites following the guidance document on relevant metabolites (SANCO/221/2000) has to be completed. In the case the trigger of 0.1 µg/L or 0.75 µg/L is exceeded there is a need to provide information on the toxicological properties and possibly consumer risk assessment (refer to 4.2 and also 2.8 and 3.3).
- The high long-term risk to mammals identified in the first tier assessment needs to be further addressed (relevant for all representative uses evaluated; data gap identified in the EPCO meeting; no submission date proposed by the applicant; refer to point 5.1)
- The risk to birds and mammals from intake of contaminated drinking water needs to be addressed (relevant for all representative uses evaluated; no submission date proposed by the applicant; refer to point 5.1)
- The ecotoxicological relevance of the photolysis metabolite DE-535 furan needs to be addressed (relevant for all representative uses evaluated; data gap identified in the EPCO meeting; no submission date proposed by the applicant; refer to point 5.2)
- A reproduction study with *Chironomus riparius*using the metabolite DE-535 pyridinol should be provided (relevant for all representative uses evaluated; data gap identified in the EPCO meeting; study submitted in April 2006 but not evaluated; refer to point 5.2)
- A risk assessment for the metabolites DE-535 pyridinol and DE-535 pyridinone that were found in concentrations >0.1 µg/L in ground water should be provided (relevant for all representative uses evaluated; data gap identified in the EPCO meeting; toxicity studies for DE-535 pyridinol were included in the DAR and a risk assessment is presented in addendum 2 of

April 2006 but has not been peer reviewed, studies with DE-535 pyridinone on aquatic organisms were submitted to the rapporteur Member State in December 2005 but has not been evaluated evaluated; refer to point 5.2)

- The pesticidal activity of the metabolites DE-535 pyridinol and DE-535 pyridinone needs to be assessed (relevant for all representative uses evaluated; data gap identified in the EPCO meeting; an assessment is available in addendum 2 of April 2006 but has not been peer reviewed; refer to point 5.2
- An earthworm reproduction study with the soil metabolite DE-535 pyridinol is required (relevant for all representative uses evaluated; data gap identified in the EPCO meeting; a study was submitted to the rapporteur Member State in February 2006 but has not been evaluated; refer to point 5.5)
- The risk to earthworms from the metabolites DE-535 pyridinone and DE-535 phenol should be addressed (relevant for all representative uses evaluated; data gap identified in the EPCO meeting; studies were submitted to the rapporteur Member State in February 2006 but have not evaluated; refer to points 5.5)
- The risk to other soil non-target macro-organisms from the metabolites DE-535 pyridinol, DE-535 pyridinone and DE-535 phenol should be addressed (relevant for all representative uses evaluated; data requirement identified before the EPCO meeting; litterbag studies with the formulation and the metabolite DE-535 has been submitted to the rapporteur Member State in December 2005 but has not evaluated; refer to points 5.6)
- The risk to soil micro-organisms from the metabolites DE-535 pyridinol, DE-535 pyridinone and DE-535 phenol should be addressed (relevant for all representative uses evaluated; data requirement identified before the EPCO meeting; studies with DE-535 pyridinol and DE-535 pyridinone were submitted in January/February 2006 but has not been evaluated; refer to points 5.7)
- The risk to non-target plants needs to be addressed (relevant for all representative uses evaluated; data requirement identified before the EPCO meeting; a study was submitted to the rapporteur Member State in March/April 2004 but has not been evaluated; refer to points 5.8)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as a herbicide as proposed by the applicant which comprises broadcast spraying to control annual and perennial grasses in carrots, fodder legumes (peas and beans), rape seed, soy bean and sugar beet at a maximum application rate up to 0.104 kg haloxyfop-R per hectare. Only the use as herbicide was evaluated during the EU peer review process.

The representative formulated product for the evaluation was "EF-1400", an emulsifiable concentrate (EC), registered under different trade names in Europe.

Whether or not sufficient enforcement methods are available for monitoring purposes depends on the final residue definitions. The reason is that none of the submitted method is enantio selective. The residues are determined as a sum parameter of both, the *R*- and the *S*-isomer. This means that for the determination of haloxyfop-R no specific enforcement method would be available.
Furthermore, it should be noted that with the available analytical methods for food, soil and water it is not possible to differentiate between residue of the acid and its salts, esters and conjugates.
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.

The toxicological studies were generally performed with pure (>98%) racemic haloxyfop or haloxyfop-R methyl ester or with neat substances. The toxicokinetic studies indicate that absorbed methyl ester will rapidly be hydrolysed to the parent acid and the S-form haloxyfop present in racemic haloxyfop will instantaneously undergo stereochemical inversion to haloxyfop-R. Therefore, the various compounds used for testing are assumed to elicit the same systemic effects following administration and these effects can be attributed to haloxyfop-R. The absorption is rapid (> 80%) and the excretion extensive. The acute oral toxicity is moderate i.e. LD_{50} is around 300 mg/kg bw and the dermal toxicity low LD_{50}> 2000 mg/kg bw, proposed classification of Xn, R22 “Harmful if swallowed” No acute inhalation toxicity studies are available. Neither racemic haloxyfop nor haloxyfop-R methyl ester was irritating to skin and haloxyfop-R methyl ester was not a sensitizer. Haloxyfop-R methyl ester is not irritating to the eye whereas racemic haloxyfop induced signs of irritation in the conjunctival sacs and iris and caused corneal opacity covering up to 100% of the cornea in all animals. Signs of irritation (corneal opacity) persisted for 21 days in un-rinsed eyes racemic haloxyfop is therefore irritating to the eye and the classification of Xi; R41 “Risk of serious damage to eyes” is proposed. The relevant short term NOAEL is 0.5 mg/kg bw/day based on the 1-year dog study which would also be said to cover the effects observed in the 90-day studies in the dog and monkey at 2 mg/kg bw/day.
There is no mutagenic or genotoxic potential for haloxyfop-R. Haloxyfop is not carcinogenic in the rat but there are hepatocellular adenomas in the highest dose in the mice associated with peroxisome proliferation.
No reproductive effects were observed at the highest dose level of 1 mg/kg bw/day, thus being a NOAEL for reproductive effects, the NOAEL for offspring toxicity is 0.065 mg/kg bw/day based on decreased body weight of f_{1a} pups after 21 days at 1 mg/kg bw/day.
The NOAEL for maternal effects is 7.5 mg/kg bw/day and the NOAEL for developmental toxicity is 7.5 mg/kg bw/day in the first study and 15 mg/kg bw/day in the second study.
No specific studies are available for the metabolites.
The acceptable daily intake (ADI) is 0.00065 mg/kg bw/day, the acceptable operator exposure level (AOEL) is 0.005 mg/kg bw/day and the acute reference dose (ARfD) is 0.075 mg/kg bw/day, with the safety factor of 100 applied.

The operator exposure was estimated using the standard models UK-POEM and the German model. The dermal absorption is 7% and 12% for the concentrate and the diluted product, respectively. The AOEL is exceeded (169%) according to the UK-POEM even with PPE (coverall) but is below according to the German model if PPE (coverall and gloves) is applied (12%). The estimated worker and bystander exposure is below the AOEL.

To investigate the residue behaviour of haloxyfop-R in plants and livestock either the haloxyfop R-isomer or the unresolved isomeric mixture or ester variants of both compounds were used.
Plant metabolism was studied following foliar application to crops representing leafy crops, root vegetables, pulses and oilseeds. Irrespective of the ester variant or whether the racemic mixture or only the R-isomer was applied, the metabolism in all the studied crops was found to be similar commencing by a rapid and almost complete degradation to haloxyfop *(R,S)* very soon after application, followed by conjugation with carbohydrates and triglycerides. These conjugates appeared to be unstable under alkaline and acidic conditions, releasing haloxyfop *(R,S)* again.
Metabolism studies with goats and hens indicated that haloxyfop *(R,S)* is excreted unmetabolised by livestock animals. In tissue and organs residues were present as haloxyfop *(R,S)* in either form, free and conjugated.
Due to the lacking isomeric specificity of the pre-registration analytical methods any possible stereochemical inversion in either direction in food of plant and animal origin could not be detected, even though it is assumed based on available data in soil and in rats that if such inversion occurs it will be most likely from the S- to the R-isomer.
A sufficient number of residue trial data with haloxyfop-R methyl according to the GAP proposed for the representative uses is available to conclude the risk assessment for consumers and to propose MRLs. From crop rotation studies it can be concluded that no significant residue levels are expected in rotational and succeeding crops following application of haloxyfop-R methyl according to the critical GAP. The residue levels that could occur in food of animal origin when crops treated with haloxyfop-R methyl are fed to animals was assessed based on livestock feeding studies and MRLs have been proposed.
The dietary risk assessment performed for different consumer groups indicates that there are no chronic and acute concerns related to dietary exposure resulting from the representative uses assessed within the peer review procedure.

The information available on the fate and behaviour in the environment was sufficient to carry out an appropriate environmental exposure assessment at the EU level. Haloxyfop-R methyl ester is rapidly hydrolysed to haloxyfop-R in soil and water. Haloxyfop-R can be considered as very low to low persistent, but its soil metabolite DE-535 pyridinol DE-535 phenol and DE-535 pyridinone are more persistent. Haloxyfop-R methyl ester and its metabolites do not show unacceptable accumulation in soil. Haloxyfop-R and DE-535 pyridinol are also major metabolites in surface water in both the water and sediment phase. A metabolite (DE-535 furan), with a chemical structure similar to dibenzofuran, was identified in the aqueous photolysis study. Because a final conclusion on the ecotoxicological and toxicological relevance of this metabolite can not be drawn, DE-535 furan needs to be addressed

with respect of surface water compartment. The available aquatic exposure assessment is appropriate for addressing the spray drift route on entry to surface water as well as the runoff/drainage contribution with a worst case input of 15% of the application rate. For the notified intended field uses, a high potential for groundwater exposure for soil metabolites DE-535 pyridinol and DE-535 pyridinone was identified. However, after the EPCO meeting it was noted that the methods used to determine degradation rates from the experimental data for all the compounds were not compatible with the method assumed by the PELMO model as recommended by the FOCUS group. Therefore, it was agreed with the rapporteur Member State that these values should be taken with caution and new POCUS groundwater modelling is required. Pending the outcome, an evaluation of the relevance of the metabolites following the guidance document on relevant metabolites has to be completed. In the case the trigger of 0.1 µg/L or 0.75 µg/L is exceeded there is a need to provide information on the toxicological properties and possibly consumer risk assessment.

The first tier risk assessment for herbivorous and insectivorous birds resulted in TER values above the Annex VI trigger indicating a low risk. For medium herbivorous and insectivorous mammals the acute risk is considered to be low, while a first tier high long-term risk was identified. The MS experts did not accept a proposed refinement using a higher endpoint from a 16-week dietary study. It was agreed to use the endpoint of 1 mg/kg bw/day from a 2-generation reproduction study. Furthermore, since the half-life for residues in vegetation was observed to be longer than the default value, residue decline data for each crop should be used in the risk assessment. The resulting TER values are foreseen to be below the Annex VI trigger indicating a high risk, and the risk to mammals needs to be further addressed.

Haloxyfop-R methyl ester is very toxic to aquatic organisms, fish being the most sensitive group of organisms. Risk mitigation comparable to 5 m buffer zones is required to meet the Annex VI trigger. The risk to aquatic organisms from the surface water metabolites haloxyfop-R and DE-535 pyridinol is considered to be low, except for sediment dwelling organisms for which a reproduction study with *Chironomus riparius* using DE-535 pyridinol is required before a full conclusion can be drawn. No information on the toxicity of the photolysis metabolite DE-535 furan is available. If an assumption of ten times higher toxicity compared to haloxyfop-R methyl ester were applied, the resulting TER value would be below the Annex VI acute trigger. Thus data to address the toxicity of this metabolite to aquatic organism is considered necessary. Two metabolites were found in concentrations >0.1 µg/L in the FOCUS ground water modelling. DE-535 pyridinol is considered to be of no ecotoxicological relevance. A conclusion regarding the relevance of DE-535 pyridinone can only be drawn once available studies have been evaluated.

The risk to bees and other non-target arthropods is low. The risk to earthworms, other soil macro-organisms and soil micro-organisms from haloxyfop-R methyl ester and haloxyfop-R is considered to be low. However, the risk to soil organisms from exposure to the persistent soil metabolites DE-535 pyridinol, DE-pyridinone and DE-535 phenol needs to be addressed. The risk to biological methods

of sewage treatment is considered to be low. No evaluated studies are available to conclude on the risk to non-target plants.

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

- PPE (gloves +coverall during application) is needed in order to have an estimated operator exposure below the AOEL (German model), refer to 2.12.
- Risk mitigation measures comparable to 5 m buffer zones are required to protect the aquatic environment (refer to point 5.2).

Critical areas of concern

- Based on preliminary information, a high potential for ground water contamination by the metabolites of haloxyfop-R methyl ester, DE-535 pyridinol and DE-535 pyridinone, when used in field is identified. However, new FOCUS modelling in line with FOCUS recommendations about the compatibility of degradation kinetics is needed. Pending the outcome an evaluation of the relevance of the metabolites following the guidance document on relevant metabolites (SANCO/221/2000) has to be completed. In the case the trigger of 0.1 µg/L or 0.75 µg/L is exceeded there is a need to provide information on the toxicological properties and possibly consumer risk assessment.
- A high first tier long-term risk to mammals was identified and needs to be further addressed.
- Haloxyfop-R methyl ester is very toxic to fish and risk mitigation measures comparable to 5 m buffer zones are required.

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

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

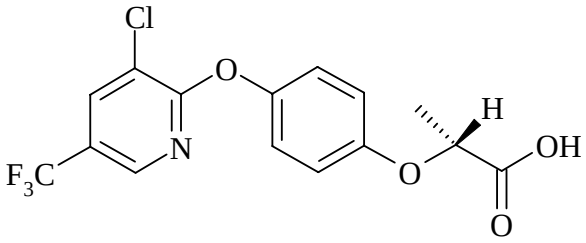
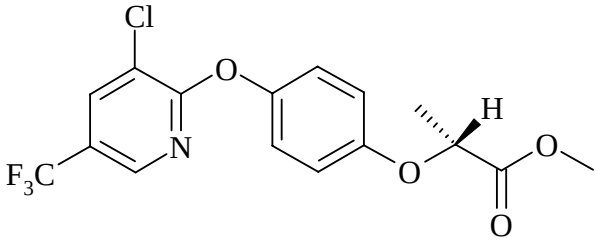
Appendix 1.1: Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Acid: haloxyfop-P. The synonym haloxyfop-R is of common use but has no official status *Ester: haloxyfop-P-methyl ester. The synonym haloxyfop-R-methyl ester is of common use but has no official status including specification to active substance, variants)*
Function (e.g. fungicide)	Herbicide
Rapporteur Member State	Denmark
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	Acid: (*R*)-2-[4-(3-chloro-5-trifluoromethyl-2-pyridyloxy)phenoxy]propanoic acid *Ester: Methyl (R)-2-[4-(3-chloro-5-trifluoromethyl-2- pyridyloxy)phenoxy]propanoic acid*
Chemical name (CA) ‡	Acid: *R*-(+)- -2-[4-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]oxy]phenoxy]propanoic acid *Ester: R-(+)-methyl-2-[4-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]oxy]phenoxy]propanoic acid*
CIPAC No ‡	Acid: 526 *Ester: 526.201*
CAS No ‡	Acid: 95977-29-0 *Ester: 72619-32-0*
EEC No (EINECS or ELINCS) ‡	Acid: not applicable *Ester: 406-250-0*
FAO Specification ‡ (including year of publication)	Acid: none *Ester: none*
Minimum purity of the active substance as manufactured ‡ (g/kg)	940g/kg (content of haloxyfop-R-methyl ester)
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	No relevant impurities

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

Molecular formula ‡	Acid: $C_{15}H_{11}ClF_3NO_4$ Ester: $C_{16}H_{13}ClF_3NO_4$
Molecular mass ‡	Acid: 361.7 Ester: 375.7
Structural formula ‡	Acid  Ester: 

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	Acid: 70.5-74.5 °C (99.3%) *Ester: -12.4 °C (98.6%)*
Boiling point (state purity) ‡	Acid: no data *Ester: estimated to >437 °C*
Temperature of decomposition	No data
Appearance (state purity) ‡	Acid: off-white powder (98.8%) *Ester: viscous light amber liquid (98.6%)*
Relative density (state purity) ‡	Acid: 1.46 g/cm^3 (98.8%) density - not relative density *Ester: 1.37 g/cm³ (98.6%) density - not relative density*
Surface tension	Acid: 41.0 mN/m *Ester: 59.87 mN/m*
Vapour pressure (in Pa, state temperature) ‡	Acid: 4.0x10^{-6} Pa at 25 °C *Ester: 5.5x10^{-5} Pa at 25 °C*

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

Henry's law constant (Pa m^3 mol^{-1}) ‡	Acid: pH5: $4.5x10^{-8}$ Pa m^3/mole pH7: $5.1x10^{-9}$ Pa m^3/mole pH9: $5.1x10^{-9}$ Pa m^3/mole *Ester:* *$1.2x10^{-3}$ Pa m^3/mole*
Solubility in water ‡ (g/L or mg/L, state temperature)	Acid: 0.375 g/L, (20 °C) unbuffered 28.2 g/L, (20 °C) pH 5 > 25%, (20 °C) pH 7 > 25%, (20 °C) pH 9 *Ester:* *9.1 mg/L, (20 °C) unbuffered* *6.9 mg/L, (20 °C) pH 5* *7.9 mg/L, (20 °C) pH 7* *at pH 9 it is claimed that the test material hydrolyse*
Solubility in organic solvents ‡ (in g/L or mg/L, state temperature)	Acid: (at 20 °C) Acetone >2000 g/L Acetonitriile >2000 g/L Ethylacetate >2000 g/L Methanol >2000 g/L Dichloroethane >1300 g/L Xylene 639 g/L *n*-octanol 1510 g/L *n*-heptane 3.93 g/L *Ester:* *Miscible up to 50 w/w at 20 °C in: Acetone, Aromatic 100, Cyclohexanone, Dichloromethane, DMF, Ethanol, Ethylacetate, Hexane, Isopropanol, Methanol, Toluene, Xylene*
Partition co-efficient (log POW) ‡ (state pH and temperature)	Acid: Experimental data: log P_{ow} pH 5: 2.82 log P_{ow} pH 7: 0.27 log P_{ow} pH 10: 0.21

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

	Estimated data: log P_{ow} pH 5: 3.18 log P_{ow} pH 7: < 0.607 log P_{ow} pH 9: 0.179 *Ester: 4.0 at 20 °C (pH-independent)*
Hydrolytic stability (DT_{50}) ‡ (state pH and temperature)	Acid: *pH 4: data requirement* pH 7: (20 °C) stable pH 9: (20 °C) stable natural water (20 °C) stable *Ester:* *pH 4: (20 °C) stable* *pH 7: (20 °C) 43 days* *pH 9: (20 °C) 0.63 day* *natural water (20 °C) 3 days*
Dissociation constant ‡	Acid: pKa=4.27 *Ester: none*
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	In acidic methanol Acid: ε $Lmol^{-1}cm^{-1}$at 274.8 nm = $1.03x10^4$ ε $Lmol^{-1}cm^{-1}$ at 223.5 nm = $1.67x10^4$ ε $Lmol^{-1}cm^{-1}$ at 202.0 nm = $2.03x10^4$ Tailing absorbance above 290 nm *Ester:* *ε $Lmol^{-1}cm^{-1}$ at 274.8 nm = $6.41x10^3$* *ε $Lmol^{-1}cm^{-1}$ at 223.5 nm = $1.63x10^4$* *ε $Lmol^{-1}cm^{-1}$ at 202.0 nm = $1.95x10^4$* *Tailing absorbance above 290 nm*
Photostability (DT_{50}) ‡ (aqueous, sunlight, state pH)	At summer sunlight 40°N, 24-hour exposure, pH 5 buffered HPLC-grade water. Acid: 12 days *Ester: 20 days* Estimated theoretical lifetime Acid: 3 days *Ester: 6 days*

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

Quantum yield of direct phototransformation in water at $\lambda > 290$ nm ‡	Acid: $\Phi = 1.7 \times 10^{-2}$ Ester: $\Phi = 3.8 \times 10^{-3}$
Flammability ‡	Acid: is not a highly flammable solid *Ester: is not a flammable liquid*
Explosive properties ‡	Acid: No risk of explodability *Ester: No risk of explodability*

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

List of representative uses evaluated (haloxyfop-R/Haloxfop-P)*

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 a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg a.s./hl min max	water L/ha min max	kg a.s./ha min max	(l)	(m)
Carrots VR 0577	S	Gallant Winner (EF-1400)	F	grasses	EC	104	Mechanical sprayer, broadcast	BBCH 14-46 (Apr-Sep)	1	N/A	0.0013-0.0052	200-400	0.052-0.104	30	[1]
Carrots VR 0577	N	Gallant Winner (EF-1400)	F	grasses	EC	104	Mechanical sprayer, broadcast	BBCH 14-50 (Apr-Sep)	1	N/A	0.0013-0.0052	200-400	0.052-0.104	56	[1]
Fodder Legumes (Beans, peas dry) VD 0071 VD 0072	N	Gallant Super (EF-1400)	F	grasses	EC	104	Mechanical sprayer, broadcast	BBCH 13-49 (Apr-Jun)	1	N/A	0.0013-0.0052	200-400	0.052-0.104	90	[1]
Rapeseed SO 0495	N	Eloge (EF-1400)	F	grasses	EC	104	Mechanical sprayer, broadcast	BBCH 12-35 (Sep-Oct)	1	N/A	0.0013-0.0052	200-400	0.052-0.104	N/S	Autumn application only [1]

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

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 a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg a.s./hl min max	water L/ha min max	kg a.s./ha min max	(l)	(m)
Rapeseed SO 0495	S	Gallant Winner (EF-1400)	F	grasses	EC	104	Mechanical sprayer, broadcast	BBCH 12-35 (Sep-Oct)	1	N/A	0.0013-0.0052	200-400	0.052-0.104	N/S	Autumn application only [1]
Soya bean VD 0541	S	Gallant Winner (EF-1400)	F	grasses	EC	104	Mechanical sprayer, broadcast	BBCH 19-33 (Apr-May)	1	N/A	0.0013-0.0052	200-400	0.052-0.104	90	[1]
Sugar beet VR 0596	N	Gallant Super (EF-1400)	F	grasses	EC	104	Mechanical sprayer, broadcast	BBCH 10-39 (Apr-Jun)	1	N/A	0.0013-0.0052	200-400	0.052-0.104	90	[1]
Sugar beet VR 0596	S	Gallant S (EF-1400)	F	grasses	EC	104	Mechanical sprayer, broadcast	BBCH 10-39 (Mar-May)	1	N/A	0.0013-0.0052	200-400	0.052-0.104	90	[1]

[1] The risk assessments revealed data gaps in section 5.

Remarks:	*	Uses for which risk assessment could not be concluded 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

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	(b)	Outdoor or field use (F), glasshouse application (G) or indoor application (I)	(j)	Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
	(c)	*e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds		
	(d)	*e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)		
	(e)	GCPF Codes - GIFAP Technical Monograph No 2, 1989	(k)	The minimum and maximum number of application possible under practical conditions of use must be provided
	(f)	Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench		
	(g)	All abbreviations used must be explained	(l)	PHI - minimum pre-harvest interval
			(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)	Enantiomer specific determination of haloxyfop-R methyl ester content of technical material is determined using an internal standard chiral specific high performance liquid chromatography (HPLC) assay. The sample is dissolved in hexane, K_2HPO_4 is added, shaked and allowed to settle. Propiophenone is used as internal standard. Analysed by HPLC-UV at 280 nm. The column used is a Chiralcel OK.
Impurities in technical as (principle of method)	Method 1: The sample is dissolved in acetonitrile and analysed by GC-FID. Method 2: The sample is dissolved in acetonitrile and analysed by HPLC-UV.
Plant protection product (principle of method)	The content of haloxyfop-R-methyl ester is determined using an internal standard chiral specific high performance liquid chromatography (HPLC) assay. The sample is dissolved in hexane/2-propanol/methanol (85/5/10). Propiophenone is used as internal standard. The sample is analysed by HPLC-UV at 280 nm. The column used is a Chiralcel OK

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 with mass selective detection (GC/MSD), gas chromatography (GC) with electron capture detection (ECD). LOQ: 0.01 – 0.05 mg/kg (haloxyfop)
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Methods for animal tissues utilise liquid chromatography with tandem mass spectrometry (LC/MS/MS) for the determination of haloxyfop acid in animal tissues, eggs, and milk. LOQ: 0.01 mg/kg (haloxyfop)
Soil (principle of method and LOQ)	Residues of haloxyfop-methyl, haloxyfop, and haloxyfop pyridinol are extracted from soil with acidic acetone. The analytes are partitioned into methyl-tertiary butyl ether (MTBE). The haloxyfop-methyl residue remaining in the MTBE is further purified using silica solid phase extraction (SPE) prior to analysis by GC/MSD using an Ultra 2 capillary column. Haloxyfop acid and pyridinol residues are partitioned into 1M sodium hydroxide. It is

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

	acidified, and the analytes are partitioned back into MTBE, which is evaporated and purified using silica SPE. Pyridinol is eluted first with 25% acetone/hexane and is reacted with BSTFA to form the trimethylsilyl ether (TMS) derivative prior to analysis by GC/MSD. Haloxyfop acid is eluted from the SPE column in a second fraction with 1% formic acid/acetone and is reacted with sulphuric acid/n-butanol to form the butyl ester, which is analysed by GC/MSD using an Ultra 2 capillary column. LOQ: 0.0005 mg/kg (haloxyfop-methyl) LOQ: 0.0001 mg/kg (haloxyfop) LOQ: 0.0001 mg/kg (haloxyfop-pyridinol)
Water (principle of method and LOQ)	Water samples are acidified, and residues of haloxyfop acid are extracted into dichloromethane. The dichloromethane is evaporated, and haloxyfop acid is reacted with sulphuric acid/*n*-butanol to form the butyl ester of haloxyfop acid, which is then partitioned into hexane. The derivative is analysed by GC-ECD using a column packed with 5% OV-225. LOQ: 0.05 µg/L (haloxyfop in drinking water) LOQ: 0.05 mg/L (haloxyfop in surface water)
Air (principle of method and LOQ)	Haloxyfop acid: A measured volume of air is drawn through a commercial Tenax two-bed configured tube. After air sampling, the front and back-up beds of the tube are separately extracted with acetone. An aliquot of the acetone solution is reacted with MSTFA to produce the trimethylsilyl ester of haloxyfop, which is analysed by GC-ECD using a SE 52 capillary column. LOQ: 0.556 µg/m^3 Haloxyfop-methyl: A measured volume of air is drawn through a mixed cellulose ester membrane filter backed up with a Chromosorb 102 tube. After air sampling, the membrane filter and sorbent tube are extracted with hexane for analysis of haloxyfop-methyl by GC-ECD using a DB-5 capillary column. No breakthrough of haloxyfop at a flow rate of 100-200 mL/minute for 8 hours. LOQ: 3 µg /m^3

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

Body fluids and tissues (principle of method and LOQ)	*Not required [substance is not classified as toxic (T) or very toxic (T+)]*

Classification and proposed labelling (Annex IIA, point 10)

With regard to physical/chemical data	None required

‡ 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 ‡	Rapid and extensive in all species tested, including humans (> 80%).
Distribution ‡	Primarily blood and liver
Potential for accumulation ‡	None
Rate and extent of excretion ‡	Species and sex dependent. In rats, excretion was mainly via urine in females and faeces in males and faster in females than males. In dogs excretion was mainly via faeces compared with urine for monkeys and humans.
Metabolism in animals ‡	Limited to ester hydrolysis/acid conjugation.
Toxicologically significant compounds ‡ (animals, plants and environment)	Animals and plants: Haloxyfop (R) methyl ester, haloxyfop (R) and conjugates of haloxyfop (R) expressed as haloxyfop (R). Environment: Haloxyfop-R methyl ester, haloxyfop-R, DE-535 pyridinol, DE-535 pyridinone

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	≥ 300 mg/kg bw	**Xn; R22**
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	
Rat LC_{50} inhalation ‡	No data – not required	
Skin irritation ‡	Non irritant	
Eye irritation ‡	Irritating to eyes (haloxyfop-R) Non irritant (haloxyfop-R methyl ester)	**Xi; R41**
Skin sensitization ‡ (test method used and result)	Non-sensitiser (Buehler and M&K tests)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Rat and mice: Liver and kidney, and RBC. Dog and monkey: liver, thyroid, kidney, serum cholesterol.
Lowest relevant oral NOAEL / NOEL ‡	0.2 mg/kg bw/day 16-day study in rat 0.2 mg/kg bw/day, 90-day studies in dog and monkey effects at 2 mg/kg bw/day 0.5 mg/kg bw/day, one year dog study

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

Lowest relevant dermal NOAEL / NOEL ‡	No data
Lowest relevant inhalation NOAEL / NOEL ‡	No data

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	No genotoxic potential

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

Target/critical effect ‡	Dose-related increased liver weight and hepatocellular changes associated with peroxisome proliferation
Lowest relevant NOAEL / NOEL ‡	0.065 mg/kg bw/day
Carcinogenicity ‡	No carcinogenic potential in the rat. Hepatocellular carcinoma in female mice associated with peroxisome proliferation

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	No reproduction toxicity at parental toxic doses (rat).
Lowest relevant reproductive NOAEL / NOEL ‡	Reproduction: 1 mg/kg bw/day Offspring: 0.065 mg/kg bw/day Parental: 1 mg/kg bw/day
Developmental target / critical effect ‡	Delayed ossification and increased resorption were observed at maternally toxic dose levels (rat). Increased resorption rate was also observed in the rabbit at maternal toxic doses levels.
Lowest relevant developmental NOAEL / NOEL ‡	Rat: Maternal: 1 mg/kg bw/day Developmental: 7.5 mg/kg bw/day Rabbit: Maternal: 7.5 mg/kg bw/day Developmental: 15 mg/kg bw/day

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

.....	No data

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

Other toxicological studies ‡ (Annex IIA, point 5.8)

Mode of action	Hepatocellular changes associated with peroxisome proliferation in rodents; non-rodents, including human hepatocytes, not affected.
Metabolites	No toxicological studies available
Impurity	No toxicological studies available

Medical data ‡ (Annex IIA, point 5.9)

.....	No data available *Data gap identified*

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.00065 mg/kg bw/day	2 year rat study and two generation study in rats	100
AOEL ‡	0.005 mg/kg bw/day	One year dog study.	100
ARfD ‡ (acute reference dose)	0.075 mg/kg bw/day	Developmental toxicity study in rabbit	100

Dermal absorption (Annex IIIA, point 7.3)

Gallant Winner/Super (EF-1400)	7% dermal absorption of the product and 12% of the diluted spray solution, based on *in vivo* data (rat).

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

Acceptable exposure scenarios (including method of calculation)

Operator	Estimated exposure (% of the AOEL). The maximum application rate is 0.104 kg/ha (tractor mounted broadcast sprayer). Model — No PPE — with PPE German — 246% — 12% UK-POEM — 1117% — 169% PPE: gloves during mixing and loading, gloves + coverall during application.
Workers	The estimated worker exposure is below the AOEL (maximum exposure up to 77% of the AOEL).
Bystanders	The estimated exposure is below the AOEL (less than 3%).

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	Xn, Xi — Harmful, irritating R22 — harmful if swallowed R41 — Risk of serious damage to eyes (only haloxyfop-R)

‡ 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	Lettuce, sugar beet, soya bean, rape, dry pea and bean
Rotational crops	Lettuce, turnip, soya bean, carrot, sugar beet and wheat
Plant residue definition for monitoring	Sum of haloxyfop-R methyl ester, haloxyfop-R (including anionic form) and conjugates of haloxyfop-R expressed as haloxyfop-R[(a)]
Plant residue definition for risk assessment	Sum of haloxyfop-R methyl ester, haloxyfop-R (including anionic form) and conjugates of haloxyfop-R expressed as haloxyfop-R
Conversion factor (monitoring to risk assessment)	None

[(a)] Optional proposal for definition: sum of haloxyfop (R,S) methyl ester, haloxyfop (R,S) and its conjugates expressed as haloxyfop (R,S).

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

Animals covered	Dairy cattle, beef cattle and hens
Animal residue definition for monitoring	Sum of haloxyfop-R and conjugates of haloxyfop-R (including anionic form) expressed as haloxyfop-R[(b)]
Animal residue definition for risk assessment	Sum of haloxyfop-R and conjugates of haloxyfop-R (including anionic form) expressed as haloxyfop-R
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes

[(b)]Optional proposal for definition: sum of haloxyfop (R,S) and its conjugates expressed as haloxyfop (R,S).

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

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

.....	At plant-back of 30 or 120 days, ≤ 0.01 mg/kg in edible parts of carrot, lettuce, turnip, sugar beet, soya beans, and wheat grain. Trace residues in wheat forage and straw that could be used for animal consumption. The low residues ingested by the animal from these commodities are sufficiently covered by the proposed MRL in animal products

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

.....	Storage stability of haloxyfop residues was demonstrated in a variety of crops representing oil-containing crops, starch-containing crops and protein-containing crops. Haloxyfop residues were found to be stable in crops stored frozen for up at least 7 months at approximately -20 °C.

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

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: yes	Poultry: no	Pig: yes
Muscle	ND (0.5 mg/kg feeding level)	<0.01 mg/kg (0.25 mg/kg feeding level)	No study required
Liver	0.03 mg/kg (0.5 mg/kg feeding level)	0.08 mg/kg (0.25 mg/kg feeding level)	
Kidney	0.11 mg/kg (0.5 mg/kg feeding level)	Not applicable	
Fat	0.01 mg/kg (0.5 mg/kg feeding level)	0.03 mg/kg (0.25 mg/kg feeding level)	
Milk	0.02 mg/kg (0.75 mg/kg feeding level)	Not applicable	
Eggs	Not applicable	ND (0.25 mg/kg feeding level)	

‡ 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)
Carrots	North South	1 x <0.01, 2 x 0.01, 1 x 0.02, 1 x 0.05 mg/kg 2 x <0.01, 2 x 0.01, 2 x 0.02, 1 x 0.04, 1 x 0.08 mg/kg	In the north three trials have been performed with a higher dose than in GAP but as the residues are <0.01, 0.01 and 0.03 it is concluded that no more trials are necessary for the northern region.	0.10	0.01
Sugar beet	North South	0.01, 3 x <0.02, 2 x 0.02, 1 x 0.03, 1 x 0.04, 0.06, 2 x 0.09 mg/kg 1 x <0.02, 1 x 0.02, 2 x 0.03,	No MRL is proposed as MRL is not established within the EU for sugar beet or sugar.		
Soya beans	South	<2 x 0.02, 4 x <0.05, 1 x 0.07 mg/kg	Intended use is only for the south.	0.10	<0.05
Rapeseed	North South	<7 x 0.05, 1 x 0.07 mg/kg 3 x <0.05mg/kg	It is not expected that residues above 0.05 will be present in rapeseed from the south so no more trials are requested. Besides the residue of 0.07 mg/kg from the north determines the MRL.	0.10	<0.05
Peas (dry)	North	4 x <0.02, 2 x 0.03, 1 x 0.06, 1 x 0.1 mg/kg	Intended use is only for the north.	0.10	0.025

(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

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

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

ADI	0.00065 mg/kg bw
TMDI (European Diet) (% ADI)	52 % (WHO, adult, 60 kg bw) 18 % (UK model, toddler, 14.5 kg bw) 13% (German model, girl, 5-7 year, 13 kg bw; animal products not included in this model)
IEDI (European diet) (% ADI)	Not required
Factors included in IEDI	Not required
ARfD	0.075 mg/kg bw/day
Acute exposure (% ARfD)	9 % (UK model, infant, 7.5 kg bw); carrot

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Sugar beets - raw juice - pressed pulp - white sugar - green syrup - molasses - molassed pulp	1 (two different dosing rates)	 0.43-0.82 0.36-0.43 N/A 2.9-3.1 18.2-18.6 7.3-8.6	 55-165 10-14 N/A 33-48
Soybeans - hulls - meal - refined oil - crude oil - soapstock	2 (three different sites)	 0.63-71 0.75-1.3 0.38-0.75 0.38-0.79 0.38-1.4	 3-9 30-70 6 3 0.2
Rape - crude oil - refined oil - meal	1 (three different dosing rates)	 1.4-2 1.1-2.2 0.9	Not possible

* 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)

Carrots	0.1
Soya bean seed	0.1

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Rapeseed	0.1
Dry peas (pulses)	0.1
Milk	0.01*[(a)]
Egg [(b)]	0.01*[(a)]
Liver, poultry [(b)]	0.05
Liver, others [(b)]	0.02
Kidney [(b)]	0.05
Fat, poultry [(b)]	0.03
Other products of animal origin [(b)]	0.01*[(a)]
Baby food and infant follow on formulae according to directive 2003/13/EF and 2003/14/EF [(b)]	0.003*[(a)]

[(a)] MRL set at the limit of quantification of the analytical method.
[(b)] not peer reviewed MRL proposal

‡ 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 ‡	20°C ^{14}C-phenyl labelling: 32 % AR after 90 days (n=1) 20°C ^{14}C-pyridine labelling: 1.0, 2.5, 2.9, 3.3 % AR after 91 days and 6.2, 6.3 % AR after 90 days (n=6) 10°C ^{14}C- pyridine labelling: 1.3 % AR after 90 days (n=1) 20°C ^{14}C-phenyl labelling, sterile: 0.2 % AR after 90 days (n=1)
Non-extractable residues after 100 days ‡	20°C ^{14}C-phenyl labelling: 44 % AR after 90 days (n=1) 20°C ^{14}C- pyridine labelling: 3.4, 31, 32, 35 % AR after 91 days and 28, 38 % AR after 90 days (n=6) 10°C ^{14}C- pyridine labelling: 33 % AR after 90 days (n=1) 20°C ^{14}C-phenyl labelling, sterile: 12 % AR after 90 days (n=1)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	Haloxyfop-R (DE-535 acid): 20°C ^{14}C-phenyl and -pyridine labelling: Range: 2.8 – 91 % AR (n=6) Max: 53 – 91 % AR (n=6) 69 – 85 % (sterile) (n=1)
	DE-535 phenol: 20°C ^{14}C- pyridine labelling: Range: 0.0 – 12.6 % AR (n=6) Max: 1.2-12.6 % AR (n=6)
	DE-535 pyridinol: 20°C ^{14}C- pyridine labelling: Range: 1.0 – 52 % AR (n=6) Max: 29-52 % AR (n=6)

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

	DE-535 pyridinone: 20°C ^{14}C- pyridine labelling: Range: 0.0 – 11.0 % AR (n=6) Max: 0.0 – 11.0 % AR (n=6)

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

Anaerobic degradation ‡	Degradation after 120 days: Haloxyfop-R methyl ester: > 99 % (n=2) Metabolites: DE-535 phenol: 33 % (n=1) DE-535 pyridinol: 72 % (n=1) DE-535 pyridinone: 26 % (n=1) Max conc. of metabolites after application of DE-535: Haloxyfop-R: 89 % (3 days) (n=2) DE-535 phenol: 0.8 % (3-7 days) (n=2) DE-535 pyridinol: 0.4 % (3 days) (n=2) DE-535 pyridinone: not detected (n=2)
Soil photolysis ‡	Photodegradation of haloxyfop-R methyl ester after irradiation for 41 equivalent sunlight days: 91 % (n=1) Degradation of haloxyfop-R in dark control: 99 % (n=1) Max conc. of metabolites after irradiation for 41 equivalent sunlight days: Haloxyfop-R: 83 % (2-25 sunlight days) (n=1) DE-535 phenol: 5 % (4.8 sunlight days) (n=1) Max conc. of metabolites in dark control: Haloxyfop-R: 92 % (2 days, approximately constant) (n=1) DE-535 phenol: 9.1 % (5 days) (n=1)

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

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

Method of calculation	<u>Aerobic studies</u> Haloxyfop-R methyl ester: first order Haloxyfop-R: first order formation and one compartment decay curve with accumulation phase or two compartment decay curve with accumulation phase DE-535 phenol: three compartment decay curve with accumulation phase or two compartment decay curve with accumulation phase DE-535 pyridinol: first order formation and one compartment decay curve with accumulation phase DE-535 pyridinone: first order formation and one compartment decay curve with accumulation phase <u>Anaerobic studies</u> Fitting of single- or two-phase exponential models with accumulation phase
Laboratory studies ‡ (range or median, with n value, with r^2 value)	<u>Haloxyfop-R methyl ester</u> 10 °C: DT_{50lab} = 0.5 d (n=1), r^2 = 0.99 DT_{90lab} = 1.7 d (n=1) 20 °C: DT_{50lab} = 0.001 - 0.6 d, average < 0.5 d (n=7) r^2 = 0.98-0.99 DT_{90lab} = 0.0033 – 1.8 d, average 0.98 d (n=7) DT_{50lab}(sterile) = 0.5 d (n=1) r^2 = 0.98 DT_{90lab}(sterile) = 1.6 d (n=1) DT_{50lab}(anaerobic) = 0.14, 0.16 d, average 0.15 d (n=2) DT_{90lab}(anaerobic) = 0.46, 0.52 d, average 0.49 d (n=2)
	<u>Haloxyfop-R</u> 10 °C: DT_{50lab} = 20.6 d (n=1) r^2 = 0.90 DT_{90lab} = 68 d (n=1) 20 °C: DT_{50lab} = 4.0 – 13 d, average 9.3 d, (n=7) r^2 = 0.92-0.99

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

DT_{90lab} = 31 – 332 d, average 128 d (n=7) DT_{50lab}(anaerobic) = 333, 842 d, average 588 (n=2) r^2 = 1 (no decimals) DT_{90lab}(anaerobic) = 1106, 3394 d, average 2250 (n=2)
DE-535 phenol 10 °C: DT_{50lab} = 44.6 d (n=1) r^2 = 0.95 DT_{90lab} = 131 (n=1) 20 °C: DT_{50lab} = 15 – 110 d, average 43 d (n=6) r^2 = 0.86-0.98 DT_{90lab} = 53 – > 365 d, average > 217 d (n=6) DT_{50lab}(anaerobic) = 281 d (n=1) r^2 = 0.994 DT_{90lab}(anaerobic) = 1088 d (n=1)
DE-535 pyridinol 10 °C: DT_{50lab} = 508 d (n=1) r^2 = 0.94 DT_{90lab} = 1615 d (n=1) 20 °C: DT_{50lab} = 79 – 437 d, average 237 d (n=6) r^2 = 0.93-0.99 DT_{90lab} = 262 – 1386 d, average > 605 d (n=6) DT_{50lab}(anaerobic) = 49 d (n=1) r^2 = 0.996 DT_{90lab}(anaerobic) = 292 d (n=1) DE-535 pyridinone 20 °C: DT_{50lab} = 205, 246 d, average 226 (n=2) r^2 = 0.93-0.95 DT_{90lab} = 475, 666 d, average 571 (n=2) DT_{50lab}(anaerobic) = 306 d (n=1) r^2 = 0.993 DT_{90lab}(anaerobic) = 1017 d (n=1)

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

Field studies ‡ (state location, range or median with n value)	Kinetics: bi-exponential model for haloxyfop-R and three-exponent model for DE- 535 pyridinol <u>Spring/summer application, 1 L/ha EF-1400</u> Haloxyfop-R Germany: DT_{50} = 12 d, DT_{90} = 119 d, r^2 = 0.999 (n=1) DT_{50} = 13 d, DT_{90} = 53 d, r^2= 0.963 (n=1) France: DT_{50} = 19 d, DT_{90} = 248 d, r^2 = 0.998 (n=1) DT_{50} = 12 d, DT_{90} = 59 d, r^2= 0.991 (n=1) DE-535 pyridinol Germany: DT_{50} = 165 d, DT_{90} = 549 d, r^2 = 0.902 (n=1) <u>Autumn application, 1 L/ha EF-1400</u> Haloxyfop-R Germany: DT_{50} = 27 d, DT_{90} = 362 d, r^2 = 0.98 (n=1) DT_{50} = 6 d, DT_{90} = 241 d, r^2= 0.99 (n=1) DT_{50} = 5 d, DT_{90} = 297 d, r^2= 0.98 (n=1) DE-535 pyridinol Germany: DT_{50} = 38 d, DT_{90} = 412 d, r^2= 0.82 (n=1) DT_{50} = 193 d, DT_{90} = 640 d, r^2= 0.72 (n=1)
Soil accumulation and plateau concentration ‡	Calculated maximum plateau concentrations found immediately after application (or metabolite peak): Haloxyfop-R methyl ester PECmax plateau = 144 µg/kg soil Haloxyfop-R PECmax plateau = 119 µg/kg soil DE-535 phenol PECmax plateau = 14.9 µg/kg soil

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

	DE-535 pyridinol PECmax plateau = 54.4 µg/kg soil DE-535 pyridinone PECmax plateau = 13.9 µg/kg soil

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence ‡ (yes / no) (if yes type of dependence)	Haloxyfop-R methyl ester: No test due to rapid hydrolysis. Haloxyfop-R: Sorption: Koc: 28.5-113.5 mL/g (n = 8) Kd: 0.31-1.59 mL/g (n = 8) Soil horizon from a lysimeter (30-60 cm): Koc: 60.4 mL/g (n=1) Soil horizon from a lysimeter (60-100 cm): Koc: 55.3 mL/g (n=1) DE-535 phenol: Sorption: Koc: 658-968 mL/g (n = 7) Kd: 6.53-17.7 mL/g (n = 7) DE-535 pyridinol: Sorption: Koc: 23.4 – 67.8 mL/g (n = 7) Kd: 0.33 – 0.80 ~~9~~ mL/g (n = 7) DE-535 pyridinone: Sorption: Koc: 18.5-46.3 mL/g (n = 7) Kd: 0.26-0.5 mL/g (n = 7)

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

Column leaching ‡	No data
Aged residues leaching ‡	No data
Lysimeter/ field leaching studies ‡	Late spring study (Fraunhofer Institut, Schmallenberg-Grafschaft,

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

Germany) Crop: sugar beet (1st year) and winter wheat (2nd year) Application rate: 112 g a.s./ha or 212 g a.s./ha Leachate: 1. year: 490 mm; 2. year: 470 mm Total % AR leached at 112 g a.s./ha: 1. year: 0.12; 2. year: 0.17 Total % AR leached at 212 g a.s./ha: 1. year: 0.38; 2. year: 0.33 Annual average µg as eq/L in leachate at 112 g a.s./ha: 1. year: 0.04; 2. year: 0.03 Annual average µg as eq/L in leachate at 212 g a.s./ha: 1. year: 0.15; 2. year: 0.16 Haloxyfop-R and DE-535 Pyridinol were < 0.02 µg/L and < 0.05 µg/L at the 112 and 212 g/ha application rate, respectively. The majority of the remaining radioactivity in the soil was contained within the top 30 cm of the soil column. <u>Spring study</u> (Covance Laboratories, Muenster, Germany) Crop: sugar beet (1st year) and winter wheat (2nd year) Application rate: 108 g a.s./ha Leachate: 1. year: 248 mm; 2. year: 634 mm Total % AR leached; lys 1: 1. year: 0.49; 2. year: 2.06 Total % AR leached; lys 2: 0.40; 2. year: 1.94 Annual average µg as eq/L in lys 1: 1. year: 0.20; 2. year: 0.34 Annual average µg as eq/L in lys 2: 1. year: 0.37; 2. year: 0.58 Haloxyfop-R methyl ester, haloxyfop-R and DE-535 phenol were each below 0.004 µg as eq/L. DE-535 pyridinol peaked at 0.011 and 0.013 µg as eq/L week 99 in lysimeter 1 and 2, respectively. Metabolite U1 = trifluoroacetic acid (TFA) with annual average concentrations of 0.044 and 0.036

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

µg/L, respectively, the first year and 0.085 and 0.082 µg/L, respectively, the second year. Autumn study (Covance Laboratories, Muenster, Germany) Crop: winter oilseed rape Application rate: 108 g a.s./ha Leachate: 1. year: 188 mm; 2. year: 494 mm Total % AR leached; 54 g a.s./ha: 1. year: 0.03; 2. year: 1.9 Total % AR leached; 108 g a.s./ha: 0.17; 2. year: 1.7 Annual average µg as eq/L; 54 g a.s./ha: 1. year: 0.035; 2. year: 0.15 Annual average µg as eq/L;108 g a.s./ha: 1. year: 0.20; 2. year: 0.67 Haloxyfop-R methyl ester and DE-535-phenol: each < 0.004 µg as eq/L. Haloxyfop-R first year average annual concentrations: 0.009 and 0.003 µg as eq/L for lysimeters treated at 54 g a.s./ha and 0.089 and 0.068 µg as eq/L for lysimeters treated at 108 g a.s./ha. Second year: Haloxyfop-R < 0.004 µg as eq/L for all lysimeters. DE-535 pyridinol, annual average concentrations: < 0.004 – 0.015 µg/L for the four lysimeters the first year and 0.006 - 0.010µg/L the second year. Trifluoroacetic acid (TFA) leached with annual average concentrations the second year at 0.048 and 0.042 µg/L, respectively, for the two lysimeters treated at 54 g a.s./ha and 0.079 and 0.076 µg TFA/L for the two lysimeters treated at 108 g a.s./ha.

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

PEC (soil) (Annex IIIA, point 9.1.3)

Method of calculation	Worst-case continuous and time weighted average soil concentrations calculated when the plateau concentration is reached. The assumptions are even distribution in the top 5 cm layer and a bulk density of 1.5 g/cm3. Spray deposition is assumed to be 100 %. No interception, no losses due to surface runoff, leaching and volatilisation. Max concentrations of the metabolites haloxyfop-R, DE-535 Phenol, DE-535 Pyridinol and DE-535 Pyridinone were set to 100, 12, 52 and 11 % as eq., respectively. Where available longest realistic field DT_{50} was used, in the other longest realistic lab DT_{50} was used. Because of the inconsistency between the the calculation model and the kinetic evaluation of the degradation rates for haloxyfop-R , DE-535 phenol and DE-535 pyridinone, only initial values can be considered valid[1].
Application rate	Maximum application rate: One time 108 g a.s./ha.

PEC (soil) in µg compound/kg.

Time Days	Haloxyfop-R methyl ester DT_{50lab} = 0.7 d		Haloxyfop-R $DT_{50field}$ = 27 d		DE-535 phenol DT_{50lab} = 110 d		DE-535 pyridinol $DT_{50field}$ = 193 d		DE-535 pyridinone DT_{50lab} = 246 d	
	PECcont	PECtwa	PECcont	PECtwa	PECcont	PECtwa	PECcont	PECtwa	PECcont	PECtwa
0	144	(144)	119.0	(119.0)	14.9	(14.9)	54.4	(54.4)	13.9	(13.9)
1	36.0	77.9	n.a.	n.a.	n.a.	n.a.	54.2	54.3	n.a.	n.a.
2	9.00	48.7	n.a.	n.a.	n.a.	n.a.	54.0	54.2	n.a.	n.a.
4	0.563	25.9	n.a.	n.a.	n.a.	n.a.	53.6	54.0	n.a.	n.a.
7	0.0088	14.8	n.a.	n.a.	n.a.	n.a.	53.0	53.7	n.a.	n.a.
28	$2.0x10^{-15}$	3.71	n.a.	n.a.	n.a.	n.a.	49.2	51.8	n.a.	n.a.
50	≈ 0	2.08	n.a.	n.a.	n.a.	n.a.	45.5	49.8	n.a.	n.a.
100	≈ 0	1.04	n.a.	n.a.	n.a.	n.a.	38.0	45.7	n.a.	n.a.
365	≈ 0	0.285	n.a.	n.a.	n.a.	n.a.	14.7	30.3	n.a.	n.a.

n.a. = not available (not required).

[1] New PECsoil calculations are not required as no risk was identified for terrestrial organisms with the initial PECsoil

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

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) ‡ (state pH and temperature)	$20^{o}C$: Haloxyfop-R methyl ester: pH 4: Stable. pH 7: DT_{50} = 43 d pH 9: DT_{50} = 0.63 d natural water, pH 8: 3 d metabolites: Haloxyfop-R: max 99.1 %AR (pH 9) unknown 1: max 2.3 %AR (pH 9) unknown 2: max 2.9 %AR (pH 7)
Photolytic degradation of active substance and relevant metabolites ‡	Xenon light source, continuous irradiation Haloxyfop-R methyl ester at $20^{o}C$, pH 5 sterile buffer: Haloxyfop-R methyl ester: DT_{50} = 20 d, DT_{90} = 67 d Haloxyfop-R: Not observed in test DE-535 furan: max. 18.6% AR (irradiated samples) Haloxyfop-R methyl ester at $20^{o}C$, natural water (pH 8.5): Haloxyfop-R methyl ester: DT_{50} = 2 d, DT_{90} = 7 d Haloxyfop-R: DT_{50} = 8 d, DT_{90} = 24 d Haloxyfop-R at $20^{o}C$, pH 5 sterile buffer: Haloxyfop-R: DT_{50} = 12 d, DT_{90} = 41 d
Readily biodegradable (yes/no)	No
Degradation in water/sediment	Two different systems meaning that n=2 for all data Kinetic: first order kinetic based on optimised rate constants from modelling with MODELMAKER. <u>Haloxyfop-R methyl ester:</u> water: DT_{50} = 0.19 – 0.28 d sediment: DT_{50} = 0.06 – 0.20 d total: DT_{50} = 0.18 – 0.24 d

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

	Haloxyfop-R: water: DT_{50} = 31.5 – 54.6 d sediment: DT_{50} = 46.2 d – > 1 year total: DT_{50} = 39.2 – 51.7 d DE-535 pyridinol: not available
Mineralization	^{14}C-phenyl labelling: 49 and 53 % after 100 days (n=1) ^{14}C-pyridinol labelling: 3.8 and 11.5 % after 100 days (n=1)
Non-extractable residues	Total amount: 21.5 – 27.2 %AR (100 d) (n=4) 4.54 % AR (30 d) (sterile system) (n=2)
Distribution in water / sediment systems (active substance) ‡	Haloxyfop-R methyl ester: ^{14}C-phenyl labelling: Water: max. 78.5-83.1% AR at 0d; ND after 7 d (n=2) Sediment: max. 5.1-8.4 % AR at 0d; ND after 7 d (n=2) ^{14}C- pyridine labelling: Water: max. 76.7-71.3% AR at 0d; ND after 2-7 d (n=2) Sediment: max. 12.0-19.0% AR at 0d; ND after 2-7 d (n=2)
Distribution in water / sediment systems (metabolites) ‡	Haloxyfop-R: ^{14}C-phenyl labelling: Water: max. 63.8-74.1% AR after 7-30 d (n=2) Sediment: max. 20.2-26.0 % AR after 30 d (n=2) ^{14}C-pyridine labelling: Water: max. 74.5-81.5% AR after 1 d (n=2) Sediment: max. 12.7-33.7 % AR after 7-14 d (n=2) DE-535 pyridinol: ^{14}C-phenyl labelling: Can not be detected with that labelling.

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

	^{14}C-pyridine labelling: Water: max. 16.8-19.7% AR after 59-100 d (n=2) Sediment: max. 6.8-16.4 % AR after 59-100 d (n=2) DE-535 phenol: ^{14}C-phenyl labelling: Water: max. 0.3-1.6% AR after 7 d (n=2) Sediment: max. 3.6-7.3 % AR after 59-100 d (n=2) ^{14}C-pyridine labelling: Water: max. 0.8-1.3% AR after 1-7 d (n=2) Sediment: max. 1.1-5.2 % AR after 100 d (n=2)

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

Method of calculation	The worst-case concentrations in surface water are calculated for a model system defined by - a water volume with a depth of 0.3 meter - one application at 108 g a.s./ha - spray drift at 1 m of 2.77 % Haloxyfop-R methyl ester: DT_{50}water = 0.28 days Haloxyfop-R: DT_{50}water = 54.6 days. Max. conversion factor = 86 % DE-535 pyridinol: DT_{50}water = 20.6 days. Max. Conversion factor = 56.24 % based on the concentration of DE-535-pyridinol (33.13%) + the precoursers haloxyfop-R (17.85%) and DE-535-phenol (5.26%). Worst-case continuous and time weighted average surface water concentrations calculated at a distance 1 m from source are shown in the table below.
Application rate	108 g a.s./ha
Main routes of entry	Spray drift of 2.77 % in a distance of 1 meter Spray drift (2.77%) and runoff/drainage (15%)

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

PEC (surface water) – spray drift

time (days)	Haloxyfop-R methyl ester		Haloxyfop-R		DE-535 pyridinol	
	DT_{50} =0.28 days		DT_{50} = 54.6 days		DT_{50} = 20.6 days	
	Actual PEC (µg/L)	TWA PEC (µg/L)	Actual PEC (µg/L)	TWA PEC (µg/L)	Actual PEC (µg/L)	TWA PEC (µg/L)
0 (initial)	0.997	(0.997)	0.960	(0.960)	0.296	(0.296)
1	0.084	0.369	0.948	0.954	0.286	0.291
2	0.007	0.200	0.936	0.948	0.277	0.286
3	0.001	0.134	0.924	0.942	0.267	0.282
4	< 0.001	0.101	0.912	0.936	0.258	0.277
7	< 0.001	0.058	0.878	0.919	0.233	0.264
14	< 0.001	0.029	0.804	0.880	0.185	0.236
21	< 0.001	0.019	0.735	0.843	0.146	0.213
28	< 0.001	0.014	0.673	0.808	0.116	0.192
42	< 0.001	0.010	0.563	0.744	0.071	0.158

PEC (surface water) – spray drift + 15% runoff/drainage

time (days)	Haloxyfop-R methyl ester		Haloxyfop-R		DE-535 pyridinol	
	DT_{50} =0.28 days		DT_{50} = 54.6 days		DT_{50} = 20.6 days	
	Actual PEC (µg/L)	TWA PEC (µg/L)	Actual PEC (µg/L)	TWA PEC (µg/L)	Actual PEC (µg/L)	TWA PEC (µg/L)
0 (initial)	6.400	(6.400)	6.160	(6.160)	1.892	(1.892)
1	0.538	2.368	6.082	6.121	1.829	1.860
2	0.045	1.284	6.006	6.082	1.770	1.829
3	0.004	0.861	5.930	6.044	1.710	1.800
4	< 0.001	0.646	5.855	6.006	1.654	1.770
7	< 0.001	0.369	5.636	5.894	1.494	1.686
14	< 0.001	0.185	5.157	5.644	1.182	1.510
21	< 0.001	0.123	4.718	5.407	0.933	1.357
28	< 0.001	0.092	4.317	5.184	0.738	1.226
42	< 0.001	0.062	3.614	4.775	0.461	1.013

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

PEC (sediment)

Method of calculation	A worst-case scenario for haloxyfop-R methyl ester, haloxyfop-R and DE-535 Pyridinol concentrations in sediment are calculated for a model system defined by - sediment depth = 5 cm - sediment bulk density = 1.3 g/cm3 - one application at 108 g a.s./ha - spray drift at 1 m of 2.77 % - contribution from run-off/erosion and/or drainage flow: 15% of the application rate, according to FOCUS step 1 (worst-case loading) - assuming 100 % of applied substance that reaches the surface water also reaches the sediment and mixes with the top 5 cm. Haloxyfop-R methyl ester DT_{50}sed = 0.20 d Haloxyfop-R: DT_{50}sed > 1 year (= 365 d). Max. Conversion factor = 86 % DE-535 pyridinol: DT_{50}sed > 1 year (= 365 d). Max. Conversion factor = 56.24 % based on the concentration of DE-535-pyridinol (33.13%) + the precoursers ~~H~~ haloxyfop-R (17.85%) and DE-535-phenol (5.26%).
Application rate	108 g a.s./ha

PEC (sediment) – 2.77% spray drift

time (days)	Haloxyfop-R methyl ester		Haloxyfop-R		DE-535 pyridinol	
	PECcont(t) (µg a.s./kg)	PECtwa(t) (µg a.s./kg)	PECcont(t) (µg a.s./kg)	PECtwa(t) (µg a.s./kg)	PECcont(t) (µg a.s./kg)	PECtwa(t) (µg a.s./kg)
0	4.43	4.43	7.61	7.61	4.99	4.99
1	0.14	1.23	7.59	7.61	4.97	4.99
2	0.00	0.64	7.58	7.59	4.97	4.97
4	$4.15x10^{-6}$	0.31	7.54	7.58	4.96	4.97
7	~0	0.19	7.51	7.56	4.93	4.96
28	~0	0.05	7.22	7.40	4.72	4.86
50	~0	0.03	6.92	7.26	4.54	4.75
100	~0	0.02	6.30	6.92	4.13	4.54

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

PEC (sediment) – 2.77% spray drift + 15% runoff/drainage

time (days)	Haloxyfop-R methyl ester		Haloxyfop-R		DE-535 pyridinol	
	PECcont(t) (µg a.s./kg)	PECtwa(t) (µg a.s./kg)	PECcont(t) (µg a.s./kg)	PECtwa(t) (µg a.s./kg)	PECcont(t) (µg a.s./kg)	PECtwa(t) (µg a.s./kg)
0	28.4	28.4	48.8	48.8	32	32
1	0.88	7.9	48.7	48.8	31.9	32.0
2	0.03	4.1	48.6	48.7	31.9	31.9
4	$2.66x10^{-5}$	2.0	48.4	48.6	31.8	31.9
7	$8.0x10^{-10}$	1.2	48.2	48.5	31.6	31.8
28	~0	0.3	46.3	47.5	30.3	31.2
50	~0	0.2	44.4	46.6	29.1	30.5
100	~0	0.1	40.4	44.4	26.5	29.1

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	**Because of the inconsistency between the the 1st order kinetic used in the FOCUS PELMO model and the kinetic evaluation of the degradation rates, the PECgw values reported below should be considered with caution and should be confirmed by new FOCUSgw modelling.** The leaching of haloxyfop-R, DE-535 Phenol, DE-535 Pyridinol and DE-535 Pyridinone to groundwater in nine European locations was modelled using the FOCUS groundwater scenarios and the Pesticide Leaching Model (FOCUSPELMO 2.2.2). The 4 scenarios modelled were: 1–winter oilseed rape (WOSR) app 28d) Autumn application to winter oilseed rape, 108 g a.s./ha, no crop interception. 2– winter oilseed rape (WOSR) app 42d) Late autumn application to winter oilseed rape, 108 g a.s./ha, no crop interception. 3-sugar beet (SB) app 28d) Spring application to sugar beet, 108 g a.s./ha, no crop interception. 4- sugar beet (SB) app 42d) Early spring application to sugar beet, 108 g a.s./ha, no crop interception. This lead to 38 runs for each of the four compounds.

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

	Haloxyfop-R: DT_{50} = 11.4 d; K_{OC} = 54 DE-535 Phenol: DT_{50} = 36.1 d; K_{OC} = 761 DE-535 Pyridinol: DT_{50} = 230 d; K_{OC} = 42 DE-535 Pyridinone: DT_{50} = 226 d; K_{OC} = 31
Application rate	108 g a.s./ha. Each metabolite was modeled separately representing worst case scenarios as "applications" at their corresponding maximum amounts seen in the laboratory studies, corrected for molecular weight differences. The maximum amounts used, expressed in % as eqv. were 100 % DE-535 acid, 36.9 % DE-535 pyridinol, 7.6 % DE-535 Phenol and 9.4 % DE-535 pyridinone. Please note from Annex B.8.6.1 that the last three maximum amounts should be corrected.

$PEC_{(gw)}$

Maximum concentration	Maximum concentrations from the many model runs have not been reported. In stead the 80th percentile annual average concentrations are giving below.
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	The 80th percentile annual average concentrations from consecutive applications for a period of 20 years were modelled. In summary the results were as follows: The calculations showed that DE-535 pyridinol exceeded the limit value of 0.1 µg a.s./L in the groundwater in all scenarios, with 80th percentile annual average PECgw in the range of 0.52 – 2.87 µg/L. Pyridinone also exceeded the limit value in all scenarios, with 80th percentile annual average PECgw in the range of 0.26 – 0.90 µg/L. The leaching of haloxyfop-R was generally < 0.001 µg/L; the highest value was 0.021 µg/L in Piacenza. DE-535 Phenol was in all cases < 0.001 µg/L. The results are listed in the table below.

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

PEC(ground water) in µg compound/L as 80th percentile annual average concentrations from consecutive applications for a period of 20 years. The 4 scenario types are explained in the text above.

Location	WOSR app 28d post emergence	WOSR app 42d post emergence	SB app 28d post emergence	SB app 14d post emergence
DE-535 acid				
Chateaudun –Irr	-	-	<0.001	<0.001
No Irr	<0.001	<0.001	<0.001	<0.001
Hamburg	0.001	0.002	<0.001	<0.001
Jokionen			<0.001	<0.001
Kremsmuenster	<0.001	<0.001	<0.001	<0.001
Okehampton	0.001	0.002	<0.001	<0.001
Piacenza – Irr			0.001	<0.001
No Irr	0.021	0.014	<0.001	<0.001
Porto	<0.001	<0.001	<0.001	<0.001
Sevilla –Irr	-	-	<0.001	<0.001
- No Irr	-	-	<0.001	<0.001
Thiva –Irr	-	-	<0.001	<0.001
- No Irr	-	-	<0.001	<0.001
DE-535 pyridinol				
Chateaudun –Irr	-	-	2.402	2.352
No Irr	2.718	2.732	2.368	2.332
Hamburg	2.774	2.835	2.793	2.767
Jokionen			2.467	2.461
Kremsmuenster	2.302	2.376	2.304	2.324
Okehampton	2.275	2.309	2.225	2.191
Piacenza – Irr	-	-	1.972	1.893
No Irr	2.581	2.571	2.853	2.872
Porto	0.954	0.975	0.705	0.716
Sevilla –Irr	-	-	0.763	0.809
- No Irr	-	-	0.517	0.555
Thiva –Irr	-	-	1.791	1.689
- No Irr	-	-	2.008	1.947

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

Location	WOSR app 28d post emergence	WOSR app 42d post emergence	SB app 28d post emergence	SB app 14d post emergence
DE-535 phenol				
Chateaudun –Irr	-	-	<0.001	<0.001
- No Irr	<0.001	<0.001	<0.001	<0.001
Hamburg	<0.001	<0.001	<0.001	<0.001
Jokionen	-	-	<0.001	<0.001
Kremsmuenster	<0.001	<0.001	<0.001	<0.001
Okehampton	<0.001	<0.001	<0.001	<0.001
Piacenza – Irr	-	-	0.001	<0.001
- No Irr	<0.001	<0.001	<0.001	<0.001
Porto	<0.001	<0.001	<0.001	<0.001
Sevilla –Irr	-	-	<0.001	<0.001
- No Irr	-	-	<0.001	<0.001
Thiva –Irr	-	-	<0.001	<0.001
- No Irr	-	-	<0.001	<0.001
DE-535 pyridinone				
Chateaudun –Irr	-	-	0.762	0.753
- No Irr	0.864	0.859	0.818	0.812
Hamburg	0.826	0.842	0.895	0.876
Jokionen	-	-	0.865	0.861
Kremsmuenster	0.737	0.732	0.757	0.758
Okehampton	0.649	0.650	0.705	0.699
Piacenza – Irr	-	-	0.601	0.571
- No Irr	0.808	0.803	0.871	0.850
Porto	0.306	0.310	0.269	0.270
Sevilla –Irr	-	-	0.294	0.306
- No Irr	-	-	0.262	0.270
Thiva –Irr	-	-	0.632	0.601
- No Irr	-	-	0.755	0.734

Irr = With irrigation, No Irr = No irrigation, - no scenario for this location/crop combination in the FOCUS shell.

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

Summary of PECgw for the two metabolites leaching above the limit value of 0.1 µg/L Range of the 80th percentile annual average concentrations for the four different application scenarios.

Scenario	DE-535 Pyridinol (µg/L)	DE-535 Pyridinone (µg/L)
Châteaudun	2.33 – 2.35	0.75 – 0.86
Hamburg	2.77 – 2.84	0.83 – 0.90
Jokioinen	2.46 – 2.47	0.86 – 0.87
Kremsmünster	2.30 – 2.38	0.73 – 0.76
Okehampton	2.19 – 2.31	0.65 – 0.71
Piacenza	1.89 – 2.87	0.57 – 0.87
Porto	0.71 – 0.98	0.27 – 0.31
Sevilla	0.52 – 0.81	0.26 – 0.31
Thiva	1.69 – 2.01	0.60 – 0.76

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

Direct photolysis in air ‡	No data
Quantum yield of direct phototransformation	No data
Photochemical oxidative degradation in air ‡	Latitude: Not stated Season: Not stated DT_{50}: 0.621 days (12-hour day).
Volatilization ‡	The volatilisation of haloxyfop-R methyl ester from soil and plant surfaces was investigated in one study. Results of the plant tests showed that 19 and 20% of the applied radioactivity had volatilised from the plant leaves after 24 hours. There was no effect of application rate. Losses from soil were lower at only 2% of applied amounts at both rates.

PEC (air)

Method of calculation	Expert judgement based on vapour pressure (5.5 x 10^{-5} Pa for haloxyfop methyl ester) and information on volatilisation from plants and soil

$PEC_{(a)}$

Maximum concentration	Negligible

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

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	Soil: haloxyfop-R methyl ester (DT 90 < 3 d), haloxyfop-R, DE-535 pyridinol, DE-535 pyridinone and DE-535 phenol Ground water: haloxyfop-R methyl ester, haloxyfop-R, DE-535 pyridinol and DE-535 pyridinone Surface water: haloxyfop-R methyl ester, haloxyfop-R and DE-535 pyridinol Air: haloxyfop-R methyl ester and haloxyfop-R

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

Soil (indicate location and type of study)	No data
Surface water (indicate location and type of study)	No data
Ground water (indicate location and type of study)	In a total of 143 samples from 101 sites in Germany and France haloxyfop[2] has not been detected (< 0.1 µg/L).
Air (indicate location and type of study)	No data

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	R53 Not readily biodegradable (cf. Annex B.8.4.4.1)

[2] As the analytical methods were not specified, it is assumed that it is intended as haloxyfop, its salts and esters.

‡ 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 ‡	LD_{50} = 300 mg a.s./kg bw
Chronic toxicity to mammals	NOAEL = 1.0 mg a.s./kg bw/day
Acute toxicity to birds ‡	LD_{50} = 1159 mg/kg bw/day (haloxyfop-R methyl ester) LD_{50} = 414 mg/kg bw (haloxyfop-R)
Dietary toxicity to birds ‡	LC_{50} > 5000 ppm ~ 1106 mg a.s./kg bw/day*
Reproductive toxicity to birds ‡	NOEC = 210 mg a.s./kg ~ 17.1 mg a.s./kg bw/day*

*) Tests performed with haloxyfop-R

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

Application rate (kg a.s./ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
Tier 1[1]					
0.108	Short grass	Herbivorous mammal	acute	114	10
0.108	Insects	Insectivorous mammal	acute	315	10
0.108	Leafy crop	Herbivorous mammal	long-term	1.6	5
0.108	Insects	Insectivorous mammal	long-term	2.9	5
0.108	Short grass	Herbivorous bird	acute	64	10
0.108	Insects	Insectivorous bird	acute	74	10
0.108	Short grass	Herbivorous bird	short term	>318	10
0.108	Insects	Insectivorous bird	short term	>352	10
0.108	Short grass	Herbivorous bird	long term	9.3	5
0.108	Insects	Insectivorous bird	long term	5.5	5

[1] At tier 1 the risk assessment was performed for birds using the standard scenarios suggested for grassland and cereals and for mammals using the leafy crop scenario in the Guidance Document on Risk Assessment for Birds and Mammals.

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

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
Lepomis macrochirus	Haloxyfop-R methyl ester	96 hr	LC_{50}	0.0884
Oncorhynchus mykiss	Haloxyfop-R	96 hr	LC_{50}	>50
Oncorhynchus mykiss	DE 535 pyridinol	96 hr	LC_{50}	37.9
Oncorhynchus mykiss	EF-1400	96 hr	LC_{50}	3.85 ~0.411 mg a.s./L
Oncorhynchus mykiss	Haloxyfop-R methyl ester	28 d	NOEC	0.0052
Pimephales promelas	Haloxyfop-R	28 d	NOEC	0.86
Daphnia magna	Haloxyfop-R methyl ester	48 hr	EC_{50}	>12.3
Daphnia magna	Haloxyfop-R	48 hr	EC_{50}	>100
Daphnia magna	DE-535 pyridinol	48 hr	EC_{50}	65.3
Daphnia magna	EF-1400	48 hr	EC_{50}	12.6 ~1.56 mg a.s./L
Daphnia magna	Haloxyfop-R methyl ester	21 d	NOEC	0.509
Daphnia magna	Haloxyfop-R	21 d	NOEC	9.6
Daphnia magna	EF-1400	21 d	NOEC	4.0 ~0.435 mg a.s./L
Chironomus riparius	Haloxyfop-R methyl ester	28 d	NOEC	2.5
Navicula pelliculosa	Haloxyfop-R methyl ester	120 hr	EC_{50}	1.72
S. capricornutum	Haloxyfop-R	96 hr	EC_{50}	47.2
S. capricornutum	DE-535 pyridinol	72 hr	EC_{50}	41.5
S. capricornutum	EF-1400	96 hr	EC_{50}	72.7 ~7.49 mg a.s./L
Lemna minor	Haloxyfop-R methyl ester	14 d	EC_{50}	3.1
Lemna minor	Haloxyfop-R	14 d	EC_{50}	5.4
Lemna gibba	DE-535 pyridinol	14 d	EC_{50}	20.3
Lemna minor	EF-1400	14 d	EC_{50}	225

Microcosm or mesocosm tests
Not submitted

‡ 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 a.s./ha)	Crop	Organism	Time-scale	Distance (m) ± 15% run-off	TER	Annex VI Trigger
EF-1400						
0.108	field	*Oncorhynchus mykiss*	96 hr	1 m run-off alone	405 63	100
0.108	field	*Daphnia magna*	48 hr	1 1+run-off	1,325 207	100
0.108	field	*Daphnia magna*	21 d	1 m 1 m + run-off	421 66	10
0.108	field	*S. capricornutum*	96 hr	1 m 1 m + run-off	7,644 1,192	10
0.108	field	*Lemna minor*	14 d	1 m 1 m + run-off	23,658 3,688	10
Haloxyfop-R methyl ester						
0.108	field	*Lepomis macrochirus*	96 hr	1 m run-off alone	89 16	100
0.108	field	*Onchorhyncus mykiss*	28 d TWA used	1 m 1 m + run-off	3,050 57	10
0.108	field	*Daphnia magna*	48 hr	1 m 1 m + run-off	>12,335 >1,923	100
0.108	field	*Daphnia magna*	21 d	1 m 1 m + run-off	510 80	10
0.108	field	*Chironomus riparius*	28 d	1 m 1 m + run-off	2507 391	10
0.108	field	*Navicula pelliculosa*	120 hr	1 m 1 m + run-off	1,725 269	10
0.108	field	*Lemna minor*	14 d	1 m 1 m + run-off	3,109 485	10
Haloxyfop-R						
0.108	field	*Oncorhynchus mykiss*	96 hr	1 m 1 m + run-off	>52,083 >8119	100

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

Application rate (kg a.s./ha)	Crop	Organism	Time-scale	Distance (m) ± 15% run-off	TER	Annex VI Trigger
0.108	field	*Pimephales promelas*	28 d	1 m 1 m + run-off	896 139	10
0.108	field	*Daphnia magna*	48 hr	1 m 1 m + run-off	>104,166 >16,237	100
0.108	field	*Daphnia magna*	21 d	1 m 1 m + run-off	10,000 1,559	100
0.108	field	*S. subspicatus*	96 hr	1 m 1 m + run-off	>49,167 >7,613	10
0.108	field	*Lemna minor*	14 d	1 m 1 m + run-off	5,625 877	10
DE-535 pyridinol						
0.108	field	*Oncorhynchus mykiss*	96 hr	1 m 1 m + run-off	128,040 20,053	100
0.108	field	*Daphnia magna*	48 hr	1 m 1 m + run-off	217,667 34,550	100
0.108	field	*S. capricornutum*	72 hr	1 m 1 m + run-off	138,333 21,957	10
0.108	field	*Lemna gibba*	14 d	1 m 1 m + run-off	67,667 10,740	10

Bioconcentration

Bioconcentration factor (BCF) (0.507 mg ts/L)‡	Whole-body BCF = 17.0
Annex VI Trigger:for the bioconcentration factor	100
Clearance time (CT_{50}) (0.507 mg ts/L) (CT_{90})	Whole body DT_{50} = 46.5 hr -
Level of residues (%) in organisms after the 14 day depuration phase	33 % (0.507 mg ts/L); 4.6 % (4.84 mg ts/L)

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

Haloxyfop-R

Acute oral toxicity ‡	> 100 µg test substance/bee
Acute contact toxicity ‡	> 100 µg test substance/bee

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

EF-1400	
Acute oral toxicity	0.87 µl EF-1400/bee ~ 96 µg a.s./bee
Acute contact toxicity	0.51 µl EF-1400/bee ~ 56 µg a.s./bee

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

Application rate (kg a.s./ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests on Haloxyfop-R				
0.108	field crops	Oral	1.1	50
0.108	field crops	Contact	1.1	50
Laboratory tests on EF-1400				
0.108	field crops	Oral	1.9	50
0.108	field crops	Contact	1.1	50

Field or semi-field tests
Not required

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

Species	Stage	Test Substance	Dose (kg a.s./ha)	Endpoint	Effect	Annex VI Trigger
Typhlodromus pyri	Glass	EF-1400	0.108	Mortality Fecundity	91 61	30%
Typhlodromus pyri	Leaves	EF-1400	0.108	Mortality Fecundity	0 4	50%
Aphidius rhopalosiphi	Glass	EF-1400	0.108 0.0057	Mortality Fecundity	100 75	30%
Aphidius rhopalosiphi	Leaves	EF-1400	0.108	Mortality Fecundity	25 0	30%
Poecilus cupreus	Sand	EF-1400	0.108	Mortality Feeding rate	0 9.7	30%
Chrysoperla carnea	Leaves	EF-1400	0.108	Mortality Fecundity	16 + 75 (increase)	30%
Aleochara bilineata	Sand	EF-1400	0.108	Mortality Fecundity	19 21	30%

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

Species	Stage	Test Substance	Dose (kg a.s./ha)	Endpoint	Effect	Annex VI Trigger
Episyrphus balteatus	Glass	EF-1020	0.108	Mortality Fecundity Viability	0 15 3	30%

Field or semi-field tests
Not required.

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

Acute toxicity: Haloxyfop-R methyl ester	LC_{50} = 672 mg a.s./kg*
Acute toxicity: Haloxyfop-R	LC_{50} = 415 mg/kg*
Acute toxicity: DE-535 pyridinone	No data available
Acute toxicity: DE-535 phenol	No data available
Acute toxicity: EF-1400	LC_{50} = 370 mg/kg ~ 40.6 mg a.s./kg
Reproductive toxicity: EF-1400	NOEC = 7.0 L/ha ~ 810 g a.s./ha
Reproductive toxicity: DE-535 pyridinol	No data available
Reproductive toxicity: DE-535 pyridinone	No data available
Reproductive toxicity: DE-535 phenol	No data available

*) The value has been corrected for the soil organic content by dividing the effect concentration by 2 as logPow > 2.

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

Application rate (kg a.s./ha)	Compound	Time-scale	TER	Annex VI Trigger
0.108 kg/ha in field crop	Haloxyfop-R methyl ester	14 d	4663	10
0.108 kg/ha in field crop	Haloxyfop-R	14 d	3487	10
0.108 kg/ha in field crop	EF-1400	14 d	282	10
0.108 kg/ha in field crop	EF-1400	8 weeks	7.5*	5

*) Based on initial PECsoil.

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

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

Nitrogen mineralization ‡	< 25% effect over 28 days at app. 3 and 16 times the intended application rate of EF-1400 (0.45 and 2.25 mg a.s./ha).
Carbon mineralization ‡	< 25% effect over 28 days at app. 3 and 16 times the intended application rate of EF-1400 (0.45 and 2.25 mg a.s./ha).

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

……	No data available

Classification and proposed labelling (Annex IIA, point 10)

With regard to ecotoxicological data	N	Harmful to the environment
	R51/R53	Very toxic to aquatic organisms, may cause long term-adverse effects in the aquatic environment

‡ 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
IESTI	international estimated short term intake
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}	etal dose, median; dosis etales 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
TS	test substance
WHO	World Health Organisation
WG	water dispersible granule
yr	year