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

clodinafop

finalised: 10 August 2005

SUMMARY

Clodinafop 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.

The Netherlands being the designated rapporteur Member State submitted the DAR on clodinafop-propargyl in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 7 November 2003. Following a quality check on the DAR, the peer review was initiated on 14 January 2004 by dispatching the DAR for consultation of the Member States and the sole applicant Syngenta. 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 25 May 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 September and October 2004.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 19 July 2005 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as post emergent herbicide as proposed by the notifier which comprises broadcast spraying to control the most important grass weeds (such as *Alopecurus*, *Avena*, *Lolium*, *Phalaris* and *Setaria*) in wheat, rye and triticale at an application rate of 60 g clodinafop-propargyl per hectare. The use in barley and oat is not recommended. Clodinafop can be used only as herbicide and it is always used together with the safener cloquintocet-mexyl, which significantly improves crop tolerance. The representative formulated product for the evaluation was TOPIK 100EC, an emulsifiable concentrate (EC). Due to the fact that the propargyl ester, a variant of clodinafop, is used in the formulated product, it should

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

be noted that the evaluated data belong to the variant clodinafop-propargyl, unless otherwise specified.

Adequate methods are available to monitor the compounds given in the respective residue definition for soil and water. In case of food of plant origin, it depends on the final residue definition due to the fact that none of the submitted methods is enantio selective, i.e. for the monitoring of clodinafop no specific method would be available. However, only single methods for the determination of residues of both isomers (*R*- and *S* as a sum parameter) are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.
Sufficient analytical method and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

In mammals, clodinafop-propargyl is rapidly and 75% absorbed (males). There was a potential for accumulation in fat. The oral LD_{50} (median lethal dose) was 1392 mg/kg bw in the male rat (proposed classification: Xn; R22). Dermal and inhalatory toxicity is low. Clodinafop-propargyl was not irritating to the skin and eyes, but has sensitising properties (proposed classification: Xi; R43). Main effects during short term oral exposure were changes in biochemical parameters indicative of liver effects and changes in haematological parameters indicative of anaemia. Clodinafop-propargyl is not genotoxic. Based on increased incidences of neoplastic changes in liver, clodinafop-propargyl demonstrated oncogenic potential in rats and mice. However, this is a species specific effect and irrelevant to classification and labelling and human risk assessment (clodinafop-propargyl is a peroxisome proliferator). There were no direct effects on reproductive performance or fertility. Clodinafop-propargyl induced delayed or absent ossification and an increase in genitourinary tract variations at doses producing effects in other general toxicity studies (some critical parameters were not measured in this study). The acceptable daily intake (ADI) is set to 0.003 mg/kg bw/day and the acute reference dose (ARfD) to 0.05 mg/kg bw, safety factor of 100. The acceptable operator exposure level (AOEL) is set to 0.026 mg/kg bw/day with safety factor of 133 (correction for 75% oral absorption). The estimated operator, worker and bystander exposure is below the AOEL for proposed uses of Topik 100 EC.

The metabolism of clodinafop-propargyl was investigated in spring wheat. It involves first a hydrolysis of the ester bond to lead to formation of clodinafop, the acid form of clodinafop-propargyl. Further degradation of the molecule consists in different cleavages and conjugation with plant sugars. No metabolite was found to present a particular toxicological concern. The possible occurrence of an isomeric conversion in the metabolism was not investigated.
As parent compound cannot be considered as a valid indicator of the presence of residues due to its fast degradation, the residue definition was established as clodinafop. The EPCO experts' meeting on residues (EPCO 15) recommended inclusion of its S isomer in the residue definition as the available validated method of analysis do not distinguish the 2 isomers. This inclusion needs to be decided at risk management level as there is no data demonstrating the actual occurrence of the S-isomer in plants and as no information is available on its intrinsic toxicological properties.

In animal metabolism, clodinafop was identified as major metabolite in all edible organs and tissues of ruminants and poultry. The analytical methodology did not allow detecting an eventual isomeric conversion.

Supervised residue trials demonstrated the absence of residues above the analytical limit of quantification (LOQ) (It should be noted that the method of analysis used in the residue trials is not isomer specific and consequently measures the sum of both isomers if they are both present). The MRL may be established at 0.02* mg/kg for wheat, rye and triticale. In succeeding and rotational crops, no residues are expected and no crop or cultivation restrictions are necessary.

Chronic and acute exposures of consumers to residues resulting from the use of clodinafop propargyl are far below the ADI and the ARfD respectively, indicating the absence of a dietary risk.

Degradation of clodinafop-propargyl in soil yields clodinafop that is further degraded. Only metabolite CGA 302371[3] was detected in amounts above the 10 % applied radioactivity (AR). Unextractable residues reached a maximum of about 58 % AR and CO_2 maximums between 33 %- 60 % AR. Under anaerobic conditions no new metabolites were identified. Degradation in natural soils proceeds mainly through enzymatic / microbial processes.

Photolysis does not contribute to the degradation of clodinafop-propargyl in soil but may contribute to the degradation of clodinafop.

Clodinafop-propargyl may be considered to be low or very low persistent in soil. The formed clodinafop is low to moderate persistent in soil and its metabolite CGA 302371 is low persistent in soil.

Results of field dissipation studies confirm the low persistence of clodinafop-propargyl and its metabolites.

Clodinafop–propargyl may be classified as medium to low mobile in soil, clodinafop and metabolite CGA 302371 may be classified as very high mobile. No relationship was observed between soil pH and adsorption of clodinafop.

Clodinafop-propargyl was instable at all the pH tested. The major hydrolysis product was clodinafop that was hydrolytically stable. The hydrolytic half life (DT_{50}) of CGA 302371 at ambient temperature may be estimated to be > 1 year.

Photolysis may contribute to the environmental degradation of clodinafop-propargyl and clodinafop in water. Clodinafop-propargyl is not readily biodegradable.

In the water / sediment studies the parent compound was quantitatively converted into clodinafop in less than one day. Clodinafop degraded in the whole system with DT_{50} values of 72 d at 20 °C. The main degradation product was CGA 302371. Metabolite CGA 193468[4] was found at amounts up to 10 % AR in the sediment (DT_{50} > 68 d). The lifetime of CGA 302371 in natural aquatic systems is likely to be controlled by photochemical degradation.

PECsw and PECsed estimations were based drift as the entry route to surface water.

[3] CGA 302371: 2-hydroxy-3-fluoro-5-chloro-pyridine
[4] CGA 193468: 4-(5-chloro-3-fluoro-2-pyridinyloxy)phenol

Predicted 80th percentile annual leachate concentrations of clodinafop-propargyl, clodinafop and metabolite CGA 302371 were below 0.1 µg / L trigger for all compounds and situations modelled with FOCUS-PEARL.
Concentrations of Clodinafop-propargyl clodinafop and its metabolites in air are likely to be negligible.
Due to the fact that no enantioselective analysis was performed during the fate and behaviour studies, racemization in the different environmental compartments may not be excluded. Therefore, S isomers of clodinafop-propargyl and clodinafop are included in the residue definition.
In case that isomerisation takes place it is assumed that the S-isomers are also formed in the ecotoxicological tests and that the endpoints deriving from the tests would cover the toxicity of the potentially formed S-isomer.

The risk to birds and mammals, aquatic organisms, bees, other non-target arthropods and earthworms from the representative use of Topik 100 EC was assessed to be low. An effect of > 25 % on soil micro-organisms was observed in a soil microbial nitrogen transformation test with the soil metabolite CGA 302371. Taking into account that CGA 302371 was formed during the test with clodinafop-propargyl (in the sandy loam soil, the same soil as was used in the soil micro-organism study, the maximum of 18.3 % was reached at 0.1 days) and that the initial PEC soil of CGA 302371 is a factor 367 lower than the treatment rate in the study with clodinafop-propargyl where no effects >25 % were observed, it is considered as unlikely that CGA 302371 would pose a high risk to soil micro-organisms. In order to support this assumption with data a new study with the metabolite CGA 302371 is proposed as a confirmatory data requirement. A new study with the metabolite CGA 302371 and soil micro-organisms was conducted by the notifier. The study was not assessed and not peer reviewed but should be taken into account at Member State level. The risk to non-target plants is considered to be low.

Key words: clodinafop, clodinafop-propargyl, 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. Clodinafop-propargyl is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating the Netherlands as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, the Netherlands submitted the report of its initial evaluation of the dossier on clodinafop, hereafter referred to as the draft assessment report, to the EFSA on 7 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 14 January 2004 to the Member States and the main notifier Syngenta 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 25 May 2004 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier was attending this meeting.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised on behalf of the EFSA by the EPCO-Team at the Federal Office for Consumer Protection and Food Safety in Braunschweig in September and October 2004. 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 19 July 2005 leading to the conclusions as laid down in this report.

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

In accordance with Article 8(7) of the amended Regulation (EC) No 451/2000, this conclusion summarises the results of the peer review on the active substance and the representative formulation

evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

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

- the comments received
- the resulting reporting table (rev. 1-2 of 2 July 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. 2-0 of 5 July 2005)

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

By the time of the presentation of this conclusion to the EU-Commission, the rapporteur Member State has made available amended parts of the draft assessment report (Volume 3, B.2, B.5-B.9, appendix; Volume 4) which take into account mostly editorial changes. Since these revised documents still contain confidential information, the documents cannot be made publicly available. However, the information given can 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

Clodinafop is the ISO common name for (*R*)-2-[4-(5-chloro-3-fluoro-2-pyridyloxy)phenoxy]propionic acid (IUPAC). Due to the fact that the propargyl ester, a variant of clodinafop, is used in the formulated product, it should be noted that the evaluated data belong to the variant clodinafop-propargyl, unless otherwise specified.

Clodinafop and clodinafop-propargyl, respectively, belong to the class of aryloxyphenoxypropionic herbicides (commonly called "FOP") such as fenoxaprop-P, fluazifop-P or haloxyfop-P. Clodinafop is taken up via leaves 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 TOPIK 100EC, an emulsifiable concentrate (EC).

The evaluated representative uses as post emergent herbicide comprise broadcast spraying to control the most important grass weeds in wheat, rye and triticale at an application rate of 60 g clodinafop-propargyl per hectare. The use in barley and oat is not recommended. Clodinafop can be used only as herbicide and it is always used together with the safener cloquintocet-mexyl, which significantly improves crop tolerance.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of clodinafop as manufactured should not be less than 950 g/kg as clodinafop-propargyl (at least 98% enaniomeric excess). At the moment no FAO specification exists. The technical material contains no relevant impurities. However, since clarification is required with respect to certain impurities to confirm the proposed maximum levels in the technical material, the specification for the technical material as a whole should be regarded as provisional at the moment.
Beside this, the assessment of the data package revealed no particular area of concern.
The main data regarding the identity of clodinafop-propargyl and its physical and chemical properties are given in appendix 1.

The content of clodinafop-propargyl and cloquintocet-mexyl in the representative formulation is 100 g/L (pure) and 25 g/L (pure), respectively.

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

Adequate methods are available to monitor the compounds given in the respective residue definition, i.e. clodinafop-propargyl, clodinafop and the respective *S*-isomers, in soil and ground water; Clodinafop and its *S*-isomer in surface water.
Whether or not sufficient enforcement methods are available to monitor food of plant origin depends on the final residue definition. 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 clodinafop no specific enforcement method would be available.

The methodology used is HPLC with UV or MS/MS 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.

An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed (see 3.2).
The recently submitted method for the determination in air was not evaluated.

The discussion in the expert meeting on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material and the acceptability of the provided analytical methods for monitoring purposes.
A recently submitted study regarding the enforcement method for the determination of residues in air was neither peer reviewed by the RMS or other MS nor discussed in an EPCO experts' meeting.

2. Mammalian toxicology

The toxicological studies were performed on clodinafop propargyl (CGA 184 927), which mean R-isomer only. No explicit toxicological data on the S-isomer (CGA 196 255) is available. Clodinafop propargyl was discussed at the EPCO experts´ meeting in October 2004 (EPCO 14).

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

Clodinafop-propargyl is rapidly and for at least for 75% absorbed in males (based on radiolabel recovered in urine, tissues, cage wash and residual carcass) within 168 hours. Oral absorption in females is higher (≥ 92%). The excretion is also rapid, mainly in the urine. Total excretion after 168 hours is higher in females (92-96%) than in males (66-85%). It is widely distributed and the highest concentration was found in fat, muscle, liver, blood and kidneys. Residues were higher in males than in females. There was a potential for accumulation in fat. Elimination from ovaries, pancreas, thymus and thyroid was slow. Clodinafop-propargyl is extensively metabolised (<0.3% remaining as clodinafop-propargyl). The major metabolites evident in the excreta were clodinafop (CGA 193469) and its taurine conjugate. The metabolites in fat were diacylglycerides and triacylglycerides of clodinafop.

At the experts´ meeting, the potential for bioaccumulation was discussed due to levels remaining in fat after 7 days and the incomplete excretion in males. The rapporteur Member State was requested to check if an adequate environmental assessment had been performed, and the list of endpoints was revised to reflect the bioaccumulation potential. This issue was checked by the rapporteur Member State after the meeting. In the DAR, the potential for bioaccumulation has already been taken into account. An adequate environmental assessment has been performed: no problems with regard to bioaccumulation. There is no issue with regard to bioaccumulation that has not been addressed and no problems have arisen. Furthermore, results of an *in vitro* study (see DAR, B.6.8) indicate that the accumulation in fat is a specific feature of rodents and that in primates a lower rate of incorporation can be expected.

2.2. ACUTE TOXICITY

The oral LD_{50} was 1392 mg/kg bw in male rats, 2271 mg/kg bw in female rats and > 2000 mg/kg bw in mice. Thus, the compound is proposed to be labelled with **Xn; R22 "Harmful if swallowed"**.
The dermal toxicity in rats is low, LD_{50} > 2000 mg/kg bw. The toxicity during inhalation in rats is also low, LC_{50} > 2.3 mg/l air (maximum attainable concentration).
Clodinafop-propargyl was not irritating to the skin and eyes, but was found to have sensitizing properties (maximisation test). Thus labelling with **Xi; R43 "May cause sensitisation by skin contact"** was proposed.

2.3. SHORT TERM TOXICITY

The short term effects of clodinafop-propargyl were studied in one 28-day study in rat, one 90-day study in rat, one 90-day study in mouse, one 90-day study in dog, and a 1-year study in dog.
The short term effects of a combination of clodinafop-propargyl and the safener cloquintocet-mexyl (ratio 4:1) were studied in one 28-day study in rat, one 90-day study in rat, and one 90-day study in dog. The dermal toxicity of clodinafop-propargyl was studied in one 28-day study in rat and the dermal toxicity of a combination of clodinafop-propargyl and cloquintocet-mexyl was studied in one 21-day study in rat.
The main effects observed were changes in biochemical parameters indicative of liver effects (rat, mouse and dog) and changes in haematological parameters indicative of anaemia (rat and dog).
The relevant oral NOAEL is 100 ppm (3.4 mg/kg bw/day) in the 1-year dog study.
Following dermal exposure to clodinafop-propargyl in the rat increased liver and thymus weights, and histopathological changes in liver and thymus were observed. No local effects were observed. The relevant dermal NOAEL for systemic effects is 50 mg/kg bw/day.
In the studies with a combination of clodinafop-propargyl and cloquintocet-mexyl comparable effects were noted, and no lower NOAELs or LOAELs were established. Based on the available studies, no synergistic or potentiating effects of clodinafop-propargyl in combination with cloquintocet-mexyl are to be expected with regard to systemic effects. However, local effects were observed after exposure to the combination. The NOAEL for local effects is 4 mg clodinafop-propargyl + 1 mg cloquintocet-mexyl/kg bw/day.

In the reporting table, two Member States proposed labeling of clodinafop-propargyl with R48/22. The rapporteur Member State proposed not to label with R48/22 (see addendum). This issue was discussed in the experts´ meeting. The meeting came to the conclusion that labeling with R48/22 was not required.

In the reporting table, one Member State commented that a possible immunotoxic action of clodinafop-propargyl and the need for additional investigations should be discussed. This issue was discussed in the experts´ meeting. It was noted that at high doses some immune parameters were affected. The meeting concluded that it was not necessary to request new studies, but that immunotoxicity could have been discussed in the DAR or addendum, e.g. "there is some evidence of immunotoxicity across all species at dose levels producing general toxicity" (see also the Addendum).

2.4. GENOTOXICITY

In the DAR, 5 *in vitro* studies and 2 *in vivo* studies have been evaluated and presented. In 6 of the 7 studies, clodinafop-propargyl was negative, both with and without metabolic activation (in the *in vitro* studies). An equivocal response was noted in a chromosome aberration test with Chinese hamster ovary cells in the presence of metabolic activation. Since no dose-response was observed and the increase in the number of aberrant cells was only noted at cytotoxic concentrations, it was concluded that clodinafop-propargyl is not clastogenic in Chinese hamster ovary cells.
Based on the results, clodinafop-propargyl is considered to be non-genotoxic.

2.5. LONG TERM TOXICITY

One long term toxicity study was performed in the rat and one in the mouse.
The main effects observed in the rat were changes in biochemical parameters indicative of liver effects, changes in haematological parameters indicative of anaemia, increased liver and kidney weights, and decreased testes and spleen weight. An increased incidence of neoplastic changes in excess of the historical control range was noted in the liver, prostate and ovary. An increased incidence of neoplastic changes within the historical control range was noted in mammary gland. However, in 2003 the notifier submitted additional reports on the findings in prostate and ovary. After independent re-evaluation, using the most recent terminology and criteria for diagnosis of neoplasia, it was concluded that there are no treatment-related neoplastic changes in prostate or ovaries (see DAR). Based on the increased incidence of neoplastic changes in liver, clodinafop-propargyl demonstrated oncogenic potential in rats. However, this is a species specific effect and irrelevant to classification and labelling and human risk assessment (see section 2.8, further studies).
One Member State commented in the reporting table that the increased incidence of oncogenic effects in mammary glands at the top dose could be related to aromatase induction. This was discussed in the experts´ meeting. The meeting noted that this was a high dose effect and that there was a 300 fold margin between the effect level and the study NOAEL. The meeting therefore agreed that no additional safety factor was required.

The main effects observed in the mouse were increased incidences of non-neoplastic and neoplastic changes in the liver. Based on the increased incidence of neoplastic changes in liver, clodinafop-propargyl demonstrated oncogenic potential in mice. However, this is a species specific effect and irrelevant to classification and labelling and human risk assessment (see below, further studies).
The relevant long term NOAEL is 10 ppm (0.32 mg/kg bw/day) in the rat, based on liver effects**.**

2.6. REPRODUCTIVE TOXICITY

One study was submitted in the dossier on rat in order to determine the reproductive effects of clodinafop-propargyl (two-generation study). The notifier submitted additional data on histopathology on kidney and liver. The data was presented and evaluated in the addendum, and discussed in the experts´ meeting. The meeting agreed that the new data supported the proposed

developmental NOAEL in the DAR. There were no direct effects on reproductive performance or fertility observed at the highest tested dose. The relevant NOAEL for reproduction was set to ≥ 1000 ppm (89 mg/kg bw/day) and the parental to 4.63 mg/kg bw/day in the rat.

In order to examine teratogenic or developmental effects of clodinafop-propargyl one study in rat and one in rabbit were presented in the DAR. Initially the rapporteur Member State suggested a relevant developmental NOAEL of 40 mg/kg bw/day, based on increased incidence of foetal variations (delayed or absent ossification) in the rat. The notifier submitted additional historical control data on the rat study and this was presented and evaluated in the addendum. It was also discussed in the addendum whether R63 might be required. The new data and labelling with R63 was discussed in the experts´ meeting. Based on the effects determined in the study, the parental NOAEL could be 160 mg/kg bw/day. However, if some of the critical parameters (liver and red blood cells) had been measured, then the parental NOAEL would likely have been 40 mg/kg bw/day or below.
There was concern over the genitourinary tract lesions. The meeting agreed that the developmental NOAEL should be 5 mg/kg bw/day, based on skeletal findings and genitourinary tract findings (see addendum). Overall the experts considered the genitourinary tract effect to be a variation rather than a malformation and felt R63 was probably not required, but final decision on classification is made by ECB.
The relevant maternal and developmental NOAEL is 160 and 5 mg/kg bw/day in the rat, respectively.
Classification as a Category 3 substance Xn; R63 "Possible risk of harm to the unborn child" is still open, to be discussed by ECB.

2.7. NEUROTOXICITY

No studies performed. There are no concerns from other studies and no studies required.

2.8. FURTHER STUDIES

Mechanistic studies were conducted to elucidate the mechanisms involved in the increased incidence of neoplastic lesions in liver in rats and mice and to assess the human relevance of these effects. Clodinafop-propargyl was shown to cause peroxisome proliferation in rodent studies. Peroxisome proliferation is a consequence of expression and activation of the α subtype of the peroxisome proliferator-activated receptor (PPAR-α). The activation of this receptor has been shown to be associated with several responses typical for peroxisome proliferators, such as hepatocellular hypertrophy, stimulation of peroxisomal fatty acid β-oxidation, induction of cytochrome P450 isoenzymes of subfamily CYP4A, and hepatocellular proliferation. Several studies were performed to confirm these effects. The mechanistic *in vitro* and *in vivo* studies in rodents confirm that clodinafop-propargyl causes a peroxisome proliferative response in rodents, ultimately leading to the formation of liver tumours, as observed in chronic toxicity studies with clodinafop-propargyl. Based on the non-genotoxic characteristics of clodinafop-propargyl and the peroxisome proliferative properties of clodinafop-propargyl, a threshold approach is applicable for the liver tumour formation in rats and mice.

Furthermore, several studies were submitted to investigate the human relevance of the observed liver effects in rodents. The *in vitro* studies confirm that humans are non-responsive to the peroxisome proliferation caused by exposure to clodinafop-propargyl or clodinafop. It is generally accepted that humans are considered to be non-responsive to the liver growth effects of peroxisome proliferators. Therefore, the observed neoplastic lesions in the liver in rodents need not to be considered for classification and labelling and human risk assessment.

2.9. MEDICAL DATA

In one plant accidental exposure to clodinafop-propargyl was reported. The injury was described as chemical burn on the skin. In another plant three cases of adverse effects were reported: feeling of empty head and sleepiness, and stinging in the eyes.

No poisoning incidents have been reported and no epidemiological studies have been performed.

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

ADI

Initially in the DAR the rapporteur Member State proposed an ADI of 0.0032 mg/kg bw/day, based on liver effects in the 2-year oral toxicity study in rats. An additional evaluation was presented in the addendum and discussed in the experts´ meeting. The meeting agreed that 0.32 mg/kg bw/day was indeed the NOAEL in the 2-year rat study. The safety factor of 100 was used.

The ADI is rounded to 0.003 mg/kg bw/day.

AOEL

The AOEL is based on the NOAEL of 3.4 mg/kg bw/day in the 1-year study in dogs with a safety factor of 100. A correction of 75% oral absorption is required, resulting safety factor 133, see section 2.1. The AOEL is based on the dog study, since comparable NOAELs and LOAELs were noted in several species and based on dose-spacing in the studies, the study in dogs was the most appropriate for the AOEL.

The AOEL is set to 0.026 mg/kg bw/day.

ARfD

Initially in the DAR the rapporteur Member State proposed an ARfD of 0.05 mg/kg bw/day, based on developmental effects in the two-generation reproduction study in rats. This was discussed in the experts´ meeting. The meeting agreed with the proposed ARfD of 0.05 based on the NOAEL of 4.63 mg/kg bw/day in the two-generation reproduction study with a safety factor of 100, but additionally considered this supported by the effects seen in the rat developmental toxicity study (NOAEL 5 mg/kg bw/day).

The ARfD is set to 0.05 mg/kg bw.

2.11. DERMAL ABSORPTION

The dermal absorption of clodinafop-propargyl in Topik 100 EC, a 10 % EC formulation, was assessed in one *in vivo* study on rat and one *in vitro* study (on human and rat skin), which are presented in the DAR. Based on the results from the studies the rapporteur Member State proposed in the DAR that the dermal absorption should be equal to 2.5% for the undiluted and 9.75% for the diluted formulation, based on the absorption evident at 72 hours (as a worst-case).

Some Member States proposed different values for dermal absorption and this was discussed in the experts´ meeting. The rapporteur Member State used the maximum time point available (72 hours), to derive the values. Regarding the skin depot (tape stripped) the rapporteur Member State considered it to be firmly bound to the stratum corneum and not systemically available. From the *in vitro* study, a ratio of 4:1 (rat: human absorption) was derived and used to adjust the *in vivo* figures. The total percentage absorbed had been used to calculate the ratio as the flux rates had not been constant. Some experts considered the rapporteur Member State approach to be slightly conservative.

The meeting agreed that **the dermal absorption for Topik 100 EC was 2.5% for the undiluted and 10% (9.75 was rounded tot 10) for the diluted formulation,** on the basis of the *in vivo* study in the rat and by using a correction factor for the *in vitro* rat/human skin comparison.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Topic 100 EC contains 100 g clodinafop-propargyl/L. Clodinafop-propargyl is always used in combination with the safener cloquintocet-mexyl, which significantly improves crop tolerances. According to the intended uses submitted by the notifier the applied doses are in the range of 0.03 to 0.06 kg a.i./ha and the application volumes range from 200 to 400 L/ha. The plant protection product is applied using tractor mounted mechanical downward spraying.

Three operator exposure studies were submitted. However, due to several shortcomings of the studies the reliability of the study results cannot be established. Therefore, exposure estimates were derived using models.

The dermal absorption value of 2.5% for the concentrate and 10% for the dilution, and the AOEL of 0.026 mg/kg bw/day are used in the calculations.

Operator exposure

The estimated operator exposure is below the AOEL of 0.026 mg/kg bw/day for proposed uses of Topic 100 EC without any PPE according to UK-POEM and German model, see table below.

Estimated operator exposure, % of AOEL (rounded values), according to calculation with UK-POEM and German model.

Application rate	No PPE UK-POEM	No PPE German model
0.06 kg a.i./ha	80%	20%

Worker exposure

Based on the use of Topic 100 EC as herbicide in small cereal grains, no intensive contact with the crop is anticipated after application and therefore a worker re-entry risk assessment is not considered necessary.

Bystander exposure

The estimated bystander exposure is below the AOEL of 0.026 mg/kg bw/day for proposed uses of Topic 100 EC without any PPE according to EUROPOEM II, see table below.

Estimated bystander exposure, % of AOEL, according to calculation with EUROPOEM II.

Application rate	No PPE EUROPOEM II
0.06 kg a.i./ha	<1%

Safener cloquintocet-mexyl

Safe uses for operator and bystander exposure to the safener cloquintocet-mexyl were calculated with and without PPE (see DAR, B.6.13).

3. Residues

Clodinafop-propargyl was discussed at the EPCO experts' meeting for residues (EPCO 15) in October 2004.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

In a first study, the metabolism of clodinafop-propargyl was investigated in spring wheat using radiolabelled substance either in the 2,6-position of the pyridinyl ring or uniformly through the phenyl ring. Following a single application at GS 22-30 of spring wheat at a rate 25% in excess of the intended application rate, total radioactive residues in forage amounted to 1.7 and 0.09 mg eq a.s./kg, 7 and 30 days after treatment respectively.

At maturity of the plant, 61 days after the treatment, straw and grains contained 0.015-0.028 and 0.006-0.019 mg eq a.s./kg, respectively, the highest values being found for the labelling in the pyridinyl ring. The fraction of the radioactivity that could not be extracted increased with time to reach 59-69% of total radioactive residues in straw and 80% in grains.

Identification of the extractable residues was carried out using HPLC, TLC, MS and NMR techniques. Traces of parent compound could only be detected in forage (0.2 % of TRR, ≤0.001 mg/kg). Beside a mixture of unidentified polar compounds, metabolites identified in the extractable fractions of forage, straw and grain were clodinafop (CGA 193469), CGA 193468[5], CGA 302371[6], CGA 214111[7], and II2 metabolite[8], either as free or conjugated forms. Due to the very low level of total radioactive residues, none of the identified metabolites was individually present at level higher than 0.001 mg/kg in straw and grains. The unextractable residues were fully characterised.

Three additional metabolism studies in spring wheat carried out with application of the test substance at less relevant growth stages of the plant confirmed these results.

The metabolic pathway of clodinafop-propargyl in plant has been established. The first step is the hydrolysis of the ester bond leading to the formation of clodinafop (CGA 193469). Next steps involve cleavage of the molecule and conjugation with sugars. The possible occurrence of an isomeric conversion in the metabolism was not investigated.

With the exception of metabolite II2, the plant metabolites were also observed in the rat metabolism. Metabolite II2, which is a hydroxylated form of clodinafop (CGA 193469), is considered to have a similar or better toxicological profile as clodinafop (CGA 193469) because it is more hydrophilic.

The residue definition for both monitoring and risk assessment proposed by the Rapporteur Member State is clodinafop (CGA 193469), as first and biologically active degradation product of clodinafop-propargyl. This proposal is supported by the fact that the parent compound is not present in the different plant parts at harvest. Given the overall very low level of other metabolites, it is not necessary to include any other compound in the residue definition neither for monitoring nor for risk assessment.

The EPCO experts' meeting proposed to include the S isomer of clodinafop in the residue definition, resulting from the fact that the method of analysis does not distinguish the R- and S- isomers of the molecule. However there is no data allowing a comparison of the toxicological properties of R- and S-isomers. Therefore it is not sure that residues found in accordance to that residue definition can be assessed according to the toxicological end points of clodinafop-propargyl. The decision to include the S-isomer in the residue definition should therefore be taken at management level, taking into account this uncertainty and the actual level of residues in cereal grains.

A total of 64 supervised residue trials were submitted for the use of clodinafop-propargyl on cereals in both Northern and Southern regions, encompassing 4 growing seasons. Residues of clodinafop

[5] CGA 193468: 4-(5-chloro-3-fluoro-2-pyridinyloxy)phenol
[6] CGA 302371: 2-hydroxy-3-fluoro-5-chloro-pyridine
[7] CGA 214111: (R)-2-(4-hydroxy-phenoxy)propionate
[8] II2 metabolite: 2-[4-(6-chloro-3-fluoro-5 hydroxy-2-pyridinyloxy) phenoxy]-propanoic acid

(CGA 193469) in grains were always below the LOQ, even under more critical conditions than the proposed representative use (later growth stage of application). Although only a fraction of these trials were carried out using the lowest validated LOQ level of 0.02 mg/kg, this level can be proposed as MRL for wheat, rye and triticale grains. In straw, measurable residues of clodinafop (CGA 193469) were found in the Northern region up to 0.17 mg/kg when the compound was applied at growth stage 39. The reliability of these results is supported by storage stability studies demonstrating the stability at -18°C of residues of clodinafop (CGA 193469) in grain and straw for at least 2 years.

Due to the very low residue level in the raw agricultural commodities when clodinafop-propargyl is used according to the GAP supported as representative use, no residues are expected in processed products.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Three rotational crop studies were submitted. In two studies, rotational crops were grown after harvest of the treated target crop (wheat) and in one study, after treatment of the bare soil.

In the first two studies, total radioactive residues were ≤ 0.001 mg eq a.s./kg in rotational lettuce, sugar beet, winter wheat and corn grown after harvest of the target crop treated with radiolabelled substance either in the pyridinyl ring or in the phenyl ring at twice the intended application rate.

In the third study, radiolabeled substance either in the pyridinyl ring or in the phenyl ring was applied on bare soil at a rate slightly exceeding the intended rate of application (1.4N) and wheat, turnips as well as mustard were planted as rotational crops 30, 92 or 270 days after the application. Total radioactive residues in wheat grains, turnip leaves and tubers were < 0.01 mg eq a.s./kg. Only wheat forage and fodder where residues amounted to maximum 0.014 and 0.018 mg eq a.s./kg respectively, were further extracted and analyzed. The extractable residues were 70% and 35% of the total radioactive residues in wheat forage and fodder respectively. A major component was identified in the extract from forage as a sugar conjugate releasing mainly CGA 302371 after enzyme hydrolysis. Clodinafop-propargyl, clodinafop (CGA 193469) and CGA 193468 were also identified at levels < 0.001 mg eq a.s./kg.

Due to the very low residue levels observed in these studies, residues are not expected in rotational crops, no residue definition is needed and no restriction for cultivation of rotational crops needs to be applied.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Taking into account a rate of incorporation of straw in animal feed of 50%, the concentration of clodinafop (CGA 193469) will not exceed 0.1 mg/kg total feed. Therefore metabolism studies are not in principle required. These studies have however been submitted and were evaluated, but no residue definition for animal products needs to be proposed.

Metabolism studies were conducted in lactating goats and laying hens with orally administered clodinafop-propargyl radiolabelled either in the pyridinyl or the phenyl ring. Although the main product the animals are exposed to through feedingstuffs is actually clodinafop rather than its propargyl ester form, these studies can be considered as relevant given the fast hydrolysis of the parent compound in animal metabolism.
The exposure rate of tested animals was 2 and 3 order of magnitude higher than the expected practical exposure of ruminants and poultry respectively. This was necessary to reach residue levels in edible organ and tissues high enough to allow their identification.

In goats clodinafop (CGA 193469) was the major metabolite in all tissues. This metabolite was either detected as such (all samples except milk), or incorporated into cholesterol esters, triacylglycerides (fat and milk) or in other conjugates. Other observed metabolites were CGA 193468 (kidney and fat), CGA 214111 (milk) and NOA 428715[9] (kidney, liver, milk). Parent compound was not detected in any of the tissues.

In hens, clodinafop (CGA 193469) was the major metabolite in all tissues. This metabolite was either detected as such (all tissues except fat), or incorporated into acylglycerides (all tissues). In fat and eggs, almost exclusively acylglycerides were detected. Other observed metabolites were CGA 193468, CGA 214111 (liver and eggs), CGA 215010[10] (liver), 5-OH-CGA 193469 (liver, muscle, eggs) and CGA 193469-pentanoic acid and its 5-hydroxylated form (liver, eggs, muscle).

As mentioned above, given the very low potential exposure of animal to clodinafop (CGA 193469), no livestock feeding studies were required.

3.3. CONSUMER RISK ASSESSMENT

The chronic dietary risk assessment has been based on the Theoretical Maximum Daily Intake (TMDI) calculation model of WHO using the WHO European typical diet and the national Dutch diet. Residues in cereal grains were considered to be 0.02 mg/kg, being the level of the LOQ. The calculations made for both diets indicated low TMDI values (less than 2% of the ADI).

A short term exposure risk assessment was carried out using the WHO methodology and the Dutch large portion consumption data for adults and 1 to 6 year old toddlers. The National Estimated Short Term Intakes were calculated to be below 1 % of the ARfD for both adults and toddlers.

In conclusion, no risk was identified neither from the chronic nor from the acute exposures to residues resulting from the use of clodinafop-propargyl according to the representative use on wheat, rye and triticale.

[9] NOA 428715: 2-(2-[4-(5-chloro-3-fluoro-pyridin-2-yloxy)-phenoxy]propionylamino)-ethanesulfonic acid
[10] CGA 215010: 2-[4-(5-chloro-3-hydroxy-pyridin-2-yloxy)-phenoxy]propionic acid

3.4. PROPOSED MRLS

Based on the available data base, a MRL of 0.02* mg/kg for wheat, rye and triticale can be proposed to cover the representative uses supported by the applicant.

4. Environmental fate and behaviour

Clodinafop-propargyl was discussed in the EPCO experts' meeting on fate and behaviour in the environment (EPCO 12) in September 2004.

Since enantioselective methods of analysis were not employed in the fate and behaviour in the environment studies, it can not be excluded that isomerization occurs in the environment as for other phenoxyalkanoic acid herbicides.[11] Therefore, enantioisomers of clodinafop-propargyl and of clodinafop should be precautionary included in the residue definition of the different environmental compartments. It should be noted that the here reported degradation rates and degradation pathways of clodinafop-propargyl and clodinafop do not take into account the potential degradation/formation to/of the S-isomers (since the analytical method does not distinguish between the R-isomers and the S-isomers). However, in case S isomer was formed it is included in the amount of substance reported as clodinafop-propargyl or clodinafop respectively and therefore the reported DT_{50} could be understood as the whole residue half-lives.

4.1. FATE AND BEHAVIOUR IN SOI

4.1.1. ROUTE OF DEGRADATION IN SOIL

The route of degradation of clodinafop-propargyl in soil was investigated under dark aerobic conditions at 25 ºC and 75 % MWHC (pF 1.8) in two studies with the same soil and the compound labelled either at the phenyl or pyridine ring. In a separate study, degradation was investigated in the same soil at 15 ºC with the phenyl labelled compound. Degradation in other three soils at 20 ºC and 40 % MWHC (pF 2.0, 2.0 and 2.7) covering the pH range between 6.0 and 7.4 was investigated in another study with the pyridine labelled compound.

First degradation step is the fast cleavage of the propargyl ester to yield the free acid **clodinafop** (CGA 193469, max 95.2 % AR after 0.1 d) that suffers further degradation including breakdown of the ether bridge between pyridine and phenyl ring. Only metabolite **CGA 302371**, max. 18.3 % AR after 0.1 d or 14.4 AR after 56 d) was detected in amounts above the 10 % AR in some of the soils performed with the pyridine labelled clodinafop-propargyl. Unextractable residues evolved to a maximum of about 58 % AR between days 28 and 84 to decrease below 50 % at the end of the corresponding studies. CO_2 evolved to a maximum of about 60 % AR after 336 d for the phenyl labelled clodinafop-propargyl and between 33 % AR and 41 % AR after 182 d for the pyridine labelled analogous.

[11] Müller, M. D. and Buser, H-R. *Environ. Sci. Technol.***1997**, *31,* 1953-1959; Buser, H-R. and Müller, M. D. *Environ. Sci. Technol.***1997**, *31,* 1960-1967.; Wink, O and Luley, U. *Pesticide Science* **1988**, *22(1)*, 31-40.

Anaerobic degradation was investigated in one study under dark conditions at 20 ºC in one flooded soil. No new metabolites were identified since, after the initial hydrolysis, clodinafop remained stable in the total system after partition between water and soil.
One acceptable photolysis in soil study is available. No new degradation products were identified. Photolysis does not contribute to the degradation of clodinafop-propargyl in the environment but may contribute to the degradation of clodinafop (from indirect evidences such as lower amount found in irradiated samples).

Up to nine field studies with the proposed formulated product including the safener cloquintocet-mexyl are available but no new metabolites are identified.

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

Rate of degradation was investigated in the same studies used for the elucidation of the degradation route. Clodinafop-propargyl hydrolyzes very fast in all microbial active soils tested and may be considered to be low or very low persistent in soil ($DT_{50\ 20\,°C\ lab}$< 0.1 – 1.5 d, $DT_{90\ 20\,°C\ lab}$ 0.1 – 4.9 d). The formed clodinafop is low to moderate persistent in soil ($DT_{50\ 20\,°C\ lab}$ = 7.4 – 18 d) and its metabolite CGA 302371 is low persistent in soil ($DT_{50\ 20\,°C\ lab}$ = 8.8 – 12 d). The fact that under sterile conditions a slower degradation is observed for clodinafop propargyl and no degradation is observed for clodinafop demonstrated that degradation in natural soils proceeds mainly through enzymatic / microbial processes.

Results of field dissipation studies confirm the low persistence of clodinafop-propargyl, clodinafop and metabolite CGA 302371. Some deficiencies were identified in these studies, but no data has been required since they are not triggered by laboratory results (DT_{50} < 60 d) and are not needed to finalize the EU risk assessment.

PEC soil for clodinafop-propargyl, clodinafop and CGA 302371 used for the assessment of the representative uses were calculated by the RMS based on worst case laboratory DT_{50} at 20 ºC and maximum amounts observed in the laboratory studies.

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

Two batch equilibrium adsorption / desorption studies with a total of seven soils were conducted for clodinafop-propargyl, three studies with a total of five soils were conducted for clodinafop and one study with three soils was conducted for metabolite CGA 302371. Additionally one study was conducted for the minor soil metabolite CGA 193468 with three soils.
Clodinafop–propargyl may be classified as medium to low mobile in soil (Koc = 252 – 2364 mL / g), clodinafop (Koc = 25 – 46.3 mL / g) and metabolite CGA 302371 (Koc = 25 – 50 mL / g) may be classified as very high mobile. Minor metabolite CGA 193468 may be classified as medium mobile in

soil (Koc = 238 – 365 mL / g). No relationship was observed between soil pH and adsorption of clodinafop.

Column and aged column leaching studies performed with clodinafop-propargyl are available. In non aged column leaching study most of the radioactivity found in the soil coarse was clodinafop. However neither clodinafop-propargyl nor clodinafop were detected in the soil segment of the aged column study. In three months field leaching study neither clodinafop-propargyl nor clodinafop was detected (LOD = 0.05 µg / L) in samples collected form 50 cm or below, however the study was not considered to represent a worst case situation due to the low rain fall.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

The hydrolytic stability of clodinafop-propargyl was studies in aqueous buffer solutions (pH 4, 5, 7 and 9) in dark at 15, 25, and 40 ºC. Clodinafop-propargyl was instable at all the pH tested. Stability was highest at pH 5 (DT_{50} at 15, 25 and 40°C 51.3, 26.8 and 12.3 days respectively), followed by pH 4 (DT_{50} at 15, 25 and 40°C 37.6, 17.9 and 7.1 days respectively), pH 7 (DT_{50} at 15, 25 and 40°C 12.9, 4.8 and 1.2 days respectively) and pH 9 (DT_{50} at 15, 25 and 40°C 0.15, 0.07 and 0.02 days respectively). The major hydrolysis product was clodinafop that was hydrolytically stable under all tested conditions.

The hydrolytic stability of CGA 302371 was studies in aqueous buffer solutions (pH 4, 7 and 8.8) in dark at 50 ºC. No degradation was observed after 5 days; therefore the hydrolytic half life at ambient temperature may be estimated to be > 1 year.

Two acceptable studies investigate the photolytic degradation of clodinafop-propargyl (labelled at the phenyl in one study and at pyridine ring in the other) in water (buffer pH 5 to minimize hydrolysis) at 25 ºC with a xenon lamp equipped with the appropriate filters to simulate natural sunlight (λ > 290 nm). In the test with the (^{14}C-phenyl label) the main transformation product was clodinafop (maximum of 6.4% AR after 14 d and 3.2% AR after 37 d). Clodinafop was in turn broken down by cleavage of the propionic acid chain to yield CGA-193468 (maximum of 6.3%). Other minor degradation products were observed in both studies, these products never exceeded 4% AR with the exception of one component that reached 6.5% AR after 30 d but declined to 1.8% AR after 37 d. The net photolysis half-life is estimated to be 20.4 days (^{14}C-phenyl label) and 24.2 days (^{14}C-pyridinyl label). It may be concluded that photolysis may contribute to the environmental degradation of clodinafop-propargyl and clodinafop in water. No new major photo-degradation products have been identified.

Clodinafop-propargyl is not readily biodegradable.

The fate clodinafop-propargyl was investigated in two studies (with clodinafop-propargyl labelled either at phenyl or pyridine ring) with two aerobic water /sediment systems, one anaerobic system (pyridine labelled) and one sterile system (pyridine labelled) in dark at 20 ºC and also at 9 ºC for one of the aerobic systems, the anaerobic and the sterile system. For the degradation of Clodinafop-propargyl in the whole system incubated at 20°C a DT_{50} value of 0.2 days was estimated. The parent compound was quantitatively converted into clodinafop (max. 78.7 % AR (water), 28.0 % AR (sediment) and 97.7 % AR (system) at 20 ºC). Clodinafop degraded in the whole system with DT_{50}

values of 72 d at 20 °C. The main degradation product was CGA 302371 (max. 32.3 % AR (water), 13.5 % AR (sediment), 45.9 % AR (system) after 119 d at 20 °C). CGA 302371 degraded in the whole system with DT_{50} values of 142 or > 68 d at 20 °C. Metabolite CGA 193468 was found at amounts up to 10 % AR in the sediment of the phenyl labelled study and half life was estimated to be > 68 d. The distribution of radioactivity in the water, the sediment and the whole system was comparable for the two labels. Hydrolysis of clodinafop-propargyl was also rapid in the sterile system but subsequent degradation of clodinafop was insignificant.

The fate of Clodinafop-propargyl (pyridine labelled) was also investigated under anaerobic conditions in the pond water/sediment system at 20°C. The pathway of degradation was similar to that under aerobic conditions but lower levels of non-extractable radioactivity and CO_2 were formed and the rate of degradation clodinafop (DT_{50} > 217 d) was lower than under aerobic conditions.

The lifetime of CGA 302371 in natural aquatic systems is likely to be controlled by photochemical degradation (estimated environmental photolysis half lives in pure water during spring and summer at 40 and 50°N 12-81 min). The contribution of photolysis to the dissipation of CGA 193468 from natural ecosystems will be less important (photolysis half lives at 40 and 50°N during spring and summer 58-321 days).

PECsw and PECsed estimations were performed by the RMS based drift as the entry route to surface water. This approach was found acceptable since clodinafop-propargyl, clodinafop, and soil metabolite CGA 302371 are not persistent in soil and other routes of entry to surface water such as run off or drainage may be considered to be negligible with respect to spray drift.

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

Concentrations of clodinafop-propargyl, clodinafop and metabolite CGA 302371 in groundwater resulting form the representative uses were predicted by the RMS with FOCUSgw scenarios in conjunction with the model FOCUS-PEARL. Predicted 80th percentile annual leachate concentrations were below 0.1 µg / L trigger for all compounds and situations modelled.

4.3. FATE AND BEHAVIOUR IN AIR

Results for photochemical oxidative degradation of Clodinafop-propargyl and clodinafop (DT_{50} 3.8-8.0 and 4.5-7.6 hours respectively), the Henry's Law constant of 2.79E-04 and <3.9E-10 $Pa \cdot m^3 \cdot mol^{-1}$ respectively and the 24 hour volatilisation results (no measurable overall loss within 24 hours), suggest that the concentrations of clodinafop-propargyl and clodinafop in air are likely to be negligible. The Henry's Law constant of CGA 302371 and CGA 193468 (2.77E-05 and 5.41E-04 $Pa \cdot m^3 \cdot mol^{-1}$ respectively) indicate that volatilisation of these compounds from the water surface will be low, and the lifetime of any volatilised CGA 302371 and CGA 193468 will be short (DT_{50} for photochemical oxidative degradation 16.2 and 5.8 hours respectively), hence concentrations in air are expected to be negligible.

5. Ecotoxicology

It can not be excluded that isomerization of clodinafop-propargyl and clodinafop occurs in the environment (see chapter 4. Environmental fate and behaviour). No isomer specific data on ecotoxicological endpoints were available. However, in case that the S-isomer is formed during the ecotox testing the toxicity of the S-isomer formed during the test was covered in the test with clodinafop-propargyl and clodinafop. The content of the S-isomers would have been added to the measured concentrations of clodinafop-propargyl and clodinafop since the analytical method did not distinguish between the R- and S-isomers.

5.1. RISK TO TERRESTRIAL VERTEBRATES

A revised risk assessment for birds and mammals according to the latest Guidance Document on Birds and Mammals (SANCO/4145/2000) was presented in an addendum (Sep. 04). The risk was calculated for an insectivorous bird, a large herbivorous bird and a small herbivorous mammal as foreseen in the above mentioned guidance document for the intended use in cereals. The TER values for acute, short-term and long term toxicity of clodinafop-propargyl to birds were well above the trigger values. The TER value for the acute risk to herbivorous mammals was above the trigger value of 10. A first tier chronic risk assessment indicated a chronic risk to mammals but the refined chronic TER value for herbivorous mammals was above the trigger value of 5.

The TER_{lt} values for the risk to birds and mammals from consumption of earthworms and fish contaminated by clodinafop-propargyl were well above the trigger value of 5 indicating a very low risk.

Clodinafop (CGA 193469) is a major metabolite in soil and water. It appears in animals as a first step in metabolising clodinafop-propargyl. Hence the toxicity of clodinafop was covered by the toxicology studies with clodinafop-propargyl. The risk to birds is considered as low since the risk for clodinafop-propargyl was low and the initial PEC values for clodinafop (CGA 193469) are lower than for clodinafop-propargyl. Long term TER values were calculated for herbivorous mammals. The results suggest a low chronic risk to herbivorous mammals.

CGA 193468 is a major metabolite in water. The risk posed to birds and mammals by consumption of contaminated drinking water and fish was assessed to be low since the acute and long term TER values for insectivorous birds and herbivorous birds and mammals were well above the trigger values.

CGA 302371 is a major soil and water metabolite. It was also detected in wheat. No toxicity studies with CGA 302371 and birds and mammals were conducted and no evidence was found that the toxicity of the metabolite was covered by studies with clodinafop-propargyl. For the calculation of TER values it was assumed that CGA 302371 has the same toxicity as clodinafop-propargyl. Acute and long term risk due to consumption of contaminated food and drinking water was assessed to be low for birds and mammals since the TER values were clearly above the Annex VI trigger values. Only in case that acute LC50 values for CGA 302371 would be 97 (birds) and 167 (mammals) times

less and/or the NOEC values would be 11 (birds) and 3.8 (mammals) times less than that of clodinafop-propargyl, the Annex VI trigger would be breached. Aquatic organisms reacted less sensible to CGA 302371 than to clodinafop-propargyl. Although this does not necessarily imply that the toxicity of CGA 302371 for birds and mammals is less than that of clodinafop-propargyl but it could be seen as an additional hint that it is unlikely that the acute and chronic toxicity of CGA 302731 is 97 times and/or 3.8 times greater than that of clodinafop-propargyl. Hence the acute and chronic risk of CGA 302371 to birds and mammals is considered to be low. The log Pow of CGA 302371 is 0.55 suggesting a low long term risk of bio-accumulation.

The toxicity of the safener cloquinocet-mexyl to birds and mammals was lower than the toxicity of clodinafop-propargyl. The content of the safener in the formulation Topik 100 EC is only 25 % of that of clodinafop-propargyl. Therefore it was concluded that the risk of the safener to birds and mammals is low. The toxicity of CGA 153443[12] (the major metabolite of cloquinocet-mexyl) was considered to be covered by the studies with cloquinocet-mexyl. The risk of CGA 153443 to birds and mammals is considered to be low since the risk for the parent was low and initial PEC values for CGA 153433 were lower than that for the parent.

5.2. RISK TO AQUATIC ORGANISMS

A low risk was shown for all tested groups of aquatic organisms for the representative uses. The acute and chronic TER values were well above the Annex VI trigger values. Aquatic plants were the most sensitive group of organisms. The lowest endpoint (based on mg a.s./L) was observed in a test with the formulation Topik 240 EC with *Glyceria maxima (14 d EC50 = 0.15 mg a.s./L)*. The formulation was comparable to the representative formulation Topik 100 EC. Since *Glyceria maxima* was more sensitive to clodinafop-propargyl than *Lemna gibba*, the endpoint from the test with *Glyceria maxima* was used in the risk assessment and compared to the PECsw intial of 0.55 µg/L. The TER value of 271 for *Glyceria maxima* is far above the Annex VI trigger value of 10 indicating a low risk to aquatic plants.

The major metabolites in water and sediment, clodinafop (CGA 193469) and CGA 302371 were less toxic than clodinafop-propargyl. The TER values for clodinafop and CGA 302371 were far above the Annex VI trigger value of 100. The metabolite CGA 193468 was only found in sediment with a maximum formation rate of 10 %. CGA 193468 was less toxic compared to clodinafop-propargyl. Therefore the risk of metabolites to aquatic organisms is considered to be low.

The acute and long term risk of the safener cloquintocet mexyl and its major metabolite CGA 153443 to aquatic organisms was assessed by the RMS as low. The acute toxicity values for fish and daphnia for cloquintocet mexyl were lower than that of clodinafop-propargyl and the content of the safener is only 25% of that of the active substance. Algae reacted 7 times more sensible to the safener than to clodinafop-propargyl. However, the TER value for algae (based on the assumption that the PECinitial

[12] CGA 153443 (metabolite of cloquinocet-mexyl):

for cloquintocet mexyl is 25% of the initial concentration of clodinafop-propargyl) is about two orders of magnitude above the TER trigger value of 10 indicating a low risk. CGA 153433 was less toxic to fish and algae than the parent. The expected initial concentrations of CGA 153433 are lower than that of cloquintocet mexyl suggesting a low risk to aquatic organisms.

The risk of bioaccumulation for clodinafop-propargyl is low because the BCF value is below the Annex VI trigger of 100 for not readily biodegradable compounds. The log P_{ow} values of -0.44 (pH 7) and 0.52 (pH 7) of clodinafop (CGA 193469) and CGA 302371 are markedly below 3 suggesting a low risk of bioaccumulation. The log P_{ow} of CGA 193468 is 3 at pH7. The BCF for CGA 193468 was calculated as 71. This metabolite appears only in sediment at a maximum formation rate of 10% therefore the risk of bioaccumulation is considered to be low.

5.3. RISK TO BEES

The acute oral and contact toxicity studies with the technical clodinafop-propargyl were considered as confirmatory only since the studies were conducted in 1987 and were not in accordance to modern guidelines (see expert meeting on ecotoxicology, EPCO 13). However a valid data set on the oral and contact toxicity were available for the lead formulation Topik 100 EC. The HQ values for oral and contact toxicity were far below the Annex VI trigger value of 50. Therefore the risk to bees is considered to be low.

5.4. RISK TO OTHER ARTHROPOD SPECIES

The risk assessment for non-target arthropods followed the ESCORT 2 scheme. A low off field risk was shown for the two indicator species *Typhlodromus pyri* and *Aphidius rhopalosiphi*. The HQ values for the in field risk were calculated to be 2.9 and 19.6 for *T. pyri* and *A. rhopalosiphi*, indicating a high in field risk at the first tier risk assessment. Therefore extended lab studies were conducted with *T. pyri*, *A. rhopalosiph* and *Aleochara bilineata.* No lethal or sublethal effects >50 % were observed at dose rates covering the application rate of the representative uses. Hence, the in-field and off-field risk to non-target arthropods is considered to be low for the representative uses.

5.5. RISK TO EARTHWORMS

Studies on the acute toxicity to earthworms from clodinafop-propargyl, clodinafop (CGA 193469), CGA 193468 and CGA 302371 and the lead formulation Topic 100 EC are available. The TER-values resulting from the endpoints derived from these studies are well above the Annex VI trigger value of VI indicating a low acute risk to earthworms for the representative use. No chronic studies were conducted since the representative use includes only one application and the DT_{90} values of clodinafop-propargyl, clodinafop (CGA 193469) and CGA 302371 are below 100 days.

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

Since the DT_{90} values for clodinafop-propargyl, clodinafop (CGA 193469), CGA 302371, the safener cloquintocet mexyl and its metabolite CGA 153433 are less than 100 days and the product is applied only once per season no additional testing with other soil non-target macro-organisms is required.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects of the lead formulation and the soil metabolite CGA 302371 were tested on soil microbial respiration and nitrogen transformation. Deviations of more than 25 % after 28 days were not observed at a treatment rate of 1.1 mg clodinafop-propargyl/kg soil, which is 28 times the initial PECsoil of 0.04 mg clodinafop-propargyl/kg. No separate study was conducted with clodinafop (CGA 193469). The EPCO experts' meeting on ecotoxicology (EPCO 13) agreed that the effects of clodinafop were covered by the studies with clodinafop-propargyl since clodinafop-propargyl is rapidly converted to CGA 193469 and therefore the risk of CGA 193469 to soil micro organisms is considered to be low. The notifier submitted a position paper to address the risk from the soil metabolite CGA 302371 for which an effect on the nitrification rate of > 25% was observed. The position paper was assessed by the RMS but not peer reviewed since it was submitted after the EPCO experts' meeting. The RMS agreed with the argument that CGA 302371 was formed during the study with clodinafop-propargyl since in the sandy loam soil, the same soil as was used in the soil micro-organism study, the maximum formation of CGA 302371 of 18.3 % was reached at 0.1 days. The initial PECsoil of CGA302371 is 0.003 mg/kg soil, a factor 367 lower than the treatment rate in the study with the parent which did not result in effects > 25 %. The RMS is of the opinion that it is unlikely that the metabolite CGA302371 poses a high risk to soil micro-organisms. The RMS proposed a new study with CGA 302371 with a longer duration than 28 days as a confirmatory data requirement. EFSA agrees to the assessment of the RMS. A new study with the metabolite CGA 302371 and soil micro-organisms was conducted by the notifier. The study (Voelkl W., 2005) was not assessed and not peer reviewed but should be taken into account at Member State level.

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

Six non target plant species (carrot, lettuce, oat, oilseed rape, onion, pea) were treated pre-emergence and in a second study post emergence with the lead formulation Topik 100 EC. Effects of > 50 % were observed post emergence in oat. The risk for non-target plants was calculated based on the ER50 for oat (= 15 g clodinafop-propargyl/ha) and on the 90th percentile spray drift at a distance of 1 metre (PEC = 1.7 g clodinafop-propargyl/ha) resulting in a TER value of 9. The TER value was above the Annex VI trigger value of 5 indicating a low risk to non-target plants.

The risk of clodinafop (CGA 193469) as a potential groundwater metabolite was discussed at the EPCO experts' meeting on ecotoxicology (EPCO 13). The RMS included the following argumentation why clodinafop (CGA 193469) is not an ecotoxicological relevant metabolite in groundwater. The concentration of clodinafop was calculated to be < 0.1 µg/L and it was less toxic to aquatic organisms than clodinafop-propargyl. However, due to the rapid degradation of clodinafop-propargyl, clodinafop should be included in the residue definition for monitoring purpose. EFSA

agrees to the argumentation of the RMS and proposes to close the data requirement from the EPCO experts' meeting.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

The effects of clodinafop-propargyl (93.6 % purity) on sewage sludge were tested in an activated sludge respiration inhibition test. The EC_{50} for respiration was > 94 mg a.s./L. Therefore the risk for biological methods of sewage treatment is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: clodinafop-propargyl, S-isomer of clodinafop propargyl[13], clodinafop, S isomer of clodinafop[14] and CGA 302371[15]

Definitions for monitoring: clodinafop-propargyl, S-isomer of clodinafop propargyl, clodinafop and S isomer of clodinafop.

Water

Ground water

Definitions for risk assessment: clodinafop-propargyl, S-isomer of clodinafop-propargyl, clodinafop, S isomer of clodinafop and CGA 302371

Definitions for monitoring: clodinafop-propargyl, S-isomer of clodinafop-propargyl, clodinafop and S isomer of clodinafop

Surface water

Definitions for risk assessment: clodinafop-propargyl (DT_{90} < 3 d), S-isomer of clodinafop-propargyl, clodinafop, S isomer of clodinafop and CGA 302371

Definitions for monitoring: clodinafop, S isomer of clodinafop

Air

Definitions for risk assessment: clodinafop-propargyl, S-isomer of clodinafop-propargyl, clodinafop and S isomer of clodinafop

Definitions for monitoring: clodinafop-propargyl, S-isomer of clodinafop-propargyl, clodinafop and S isomer of clodinafop

[13] S-isomer of clodinafop-propargyl: prop-2-ynyl (*S*)-2-[4-(5-chloro-3-fluoro-pyridin-2-yloxy)-phenoxy]-propionionate

[14] S isomer of clodinafop: (*S*)-2-[4-(5-chloro-3-fluoro-pyridin-2-yloxy)-phenoxy]-propionionic acid

[15] CGA 302371: 5-chloro-3-fluoro-1H-pyrimidin-2-one

Food of plant origin

Definitions for risk assessment: clodinafop or sum of clodinafop and its *S* isomer expressed as clodinafop (decision to be taken at risk management level)

Definitions for monitoring: clodinafop or sum of clodinafop and its S isomer expressed as clodinafop (decision to be taken at risk management level)

Food of animal origin

Definitions for risk assessment: not required

Definitions for monitoring: not required

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Clodinafop-propargyl*	Very low to low persistent $DT_{50\ 20\,°C\ lab}$< 0.1 – 1.5 d; $DT_{90\ 20\,°C\ lab}$ = 0.1 – 4.9 d	See points 5.5., 5.6., 5.7.
Clodinafop* (CGA 193469)	Low to moderate persistent ($DT_{50\ 20\,°C\ lab}$ = 7.4 – 18 d)	The risk to earthworms is lower than that of clodinafop-propargyl and the risk to soil-non target organisms is considered to be low.
CGA 302371	Low persistent in soil ($DT_{50\ 20\,°C\ lab}$ = 8.8 – 12 d)	The risk to earthworms is lower than that of clodinafop-propargyl and the risk to soil-non target organisms is considered to be low.

* Formation of S-isomers of clodinafop-propargyl and or clodinafop cannot be excluded by available studies. In case these isomers were formed the degradation DT_{50} reported would represent the whole residue (R+S isomers) degradation rates.

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
Clodinafop-propargyl*	medium to low (Koc = 252 –	FOCUS: No	yes	Yes	Yes

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
	2364 mL / g)				
Clodinafop* (CGA 193469)	very high (Koc = 25 – 46.3 mL / g)	FOCUS: No	yes	Yes Clodinafop is the major metabolite of. clodinafop-proprgyl that remains to <0.3%.	The risk to aquatic organisms is less than that of clodinafop-propargyl, except the chronic risk to *Daphnia magna*. However, the chronic risk from clodinafop to *Daphnia magna* is considered to be low.
CGA 302371	very high (Koc = 25 – 50 mL / g)	FOCUS: No	No data available No data required	No data available No data required	The risk to aquatic organisms is less than that of clodinafop-propargyl

* Formation of S-isomers of clodinafop-propargyl and or clodinafop cannot be excluded by available studies. In case these isomers were formed the degradation DT50 reported would represent the whole residue (R+S isomers) degradation rates.

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Clodinafop-propargyl* (water and sediment) (DT_{90} < 3 d)	See point 5.2.

Compound (name and/or code)	Ecotoxicology
Clodinafop* (water and sediment) (CGA 193469)	The risk to aquatic organisms is less than that of clodinafop-propargyl, except the chronic risk to *Daphnia magna*. However, the chronic risk from clodinafop to *Daphnia magna* is considered to be low.
CGA 302371 (water and sediment)	The risk to aquatic organisms is less than that of clodinafop-propargyl
CGA 193468 (sediment only)	The risk to aquatic organisms is less than that of clodinafop-propargyl

* Formation of S-isomers of clodinafop-propargyl and or clodinafop cannot be excluded by available studies. In case these isomers were formed the degradation DT50 reported would represent the whole residue (R+S isomers) degradation rates

Air

Compound (name and/or code)	Toxicology
Clodinafop-propargyl*	Not toxic during single exposure, see 2.2.
Clodinafop* (CGA 193469)	See clodinafop propargyl. Clodinafop is the major metabolite of. clodinafop-proprgyl that remains to <0.3%.

* Although more unlikely than for other compartments, formation of S-isomers of clodinafop-propargyl and or clodinafop cannot be excluded by available studies. In case these isomers were formed the degradation DT_{50} reported would represent the whole residue (R+S isomers) degradation rates

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

- Clarification with respect to the proposed maximum levels for certain impurities in the technical material (date of submission unknown, data requirement identified by RMS in addendum 2 to Volume 4, August 2004 and confirmed by expert meeting, September 2004; refer to chapter 1)
- Analytical method for the determination of residues in air (received by the RMS but not evaluated, refer to chapter 1)
- An enantio selective method for the determination of residues in food of plant origin provided that the residue definition includes clodinafop only (with the available methods the residues are determined as a sum parameter of both, the *R*-isomer clodinafop and its *S*-isomer)
- Metabolism studies in plants investigating the possibility of isomeric conversion of the R-isomer to the S-isomer, and if relevant, toxicological studies on the S-isomer (data requirement if final residue definition contains both isomers)
- A new study with the metabolite CGA 302371 and soil micro-organisms is proposed as a confirmatory data requirement. Meanwhile this study was conducted by the notifier. W. Voelkl (2005): Determination of effects of CGA302371 (metabolite of CGA184927) on soil microflora activity. Syngenta Report 2031754.

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as post emergent herbicide as proposed by the notifier which comprises broadcast spraying to control the most important grass weeds (such as *Alopecurus*, *Avena*, *Lolium*, *Phalaris* and *Setaria*) in wheat, rye and triticale at an application rate of 60 g clodinafop-propargyl per hectare. The use in barley and oat is not recommended. Clodinafop can be used only as herbicide and it is always used together with the safener cloquintocet-mexyl, which significantly improves crop tolerance. The representative formulated product for the evaluation was TOPIK 100EC, an emulsifiable concentrate (EC). Due to the fact that the propargyl ester, a variant of clodinafop, is used in the formulated product, it should be noted that the evaluated data belong to the variant clodinafop-propargyl, unless otherwise specified.

Adequate methods are available to monitor the compounds given in the respective residue definition for soil and water. In case of food of plant origin, it depends on the final residue definition due to the fact that none of the submitted methods is enantio selective, i.e. for the monitoring of clodinafop no specific method would be available. However, only single methods for the determination of residues of both isomers (*R*- and *S* as a sum parameter) are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.
Sufficient analytical method and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

Clodinafop-propargyl is rapidly and at least 75% is absorbed (males). It is widely distributed and the highest concentration was found in fat, muscle, liver, blood and kidneys. There was a potential for accumulation in fat. Clodinafop-propargyl is extensively metabolised.

The oral LD_{50} was 1392 mg/kg bw in the male rat, proposed labelling **Xn; R22 "Harmful if swallowed"**. Dermal and inhalatory toxicity is low. Clodinafop-propargyl was not irritating to the skin and eyes, but displayed sensitising properties and should be labelled with **Xi; R43 "May cause sensitisation by skin contact"**.

The relevant oral short term NOAEL is 3.4 mg/kg bw/day in the 1-year dog study, based on changes in biochemical parameters indicative of liver effects and changes in haematological parameters indicative of anaemia. The relevant dermal NOAEL is 50 mg/kg bw/day. No synergistic or potentiating effects of a combination of clodinafop-propargyl and the safener cloquintocet-mexyl are to be expected with regard to systemic effects.

There was no evidence of genotoxicity of clodinafop-propargyl.

Based on increased incidences of neoplastic changes in liver, clodinafop-propargyl demonstrated oncogenic potential in rats and mice. However, this is a species specific effect and irrelevant to classification and labelling and human risk assessment (clodinafop-propargyl is a peroxisome proliferator).

There were no direct effects on reproductive performance or fertility observed at the highest tested dose. The relevant NOAEL for reproduction was set to 89 mg/kg bw/day and the parental to 4.63 mg/kg bw/day in the rat.

Clodinafop-propargyl induced delayed or absent ossification and an increase in genitourinary tract variations at doses producing effects in other general toxicity studies (some critical parameters were not measured in this study). The relevant developmental NOAEL is 5 mg/kg bw/day in the rat. **Classification as a Category 3 substance T; R63 is probably not required, but should be discussed at ECB.**

There were no indications of (delayed) neurotoxicity.

The ADI is set to 0.003 mg/kg bw/day, based on the NOAEL of 0.32 mg/kg bw/day in the 2-year rat study. **The AOEL is set to 0.026 mg/kg bw/day** based on the NOAEL of 3.4 mg/kg bw/day in the 1-year dog study with a safety factor of 133 for correction for 75% oral absorption. **The ARfD is set to 0.05 mg/kg bw**, based on the NOAEL of 4.63 mg/kg bw/day in the two-generation reproduction study and the NOAEL of 5 mg/kg bw/day in the rat developmental toxicity study.

The dermal absorption of clodinafop-propargyl in the formulation Topic 100 EC was 2.5% for the concentrate and 10% for the dilution.

The outcome of the risk assessment for the plant protection product Topic 100 EC, an emulsifiable concentrate containing 100 g clodinafop-propargyl/L, showed that **the estimated exposure of the operator, worker and bystander was below the AOEL without PPE (according to UK POEM and German model)**.

The metabolism of clodinafop-propargyl was investigated in spring wheat. It involves first a hydrolysis of the ester bond to lead to formation of clodinafop, the acid form of clodinafop-propargyl.

Further degradation of the molecule consists in different cleavages and conjugation with plant sugars. No metabolite was found to present a particular toxicological concern. The possible occurrence of an isomeric conversion in the metabolism was not investigated.

As parent compound cannot be considered as a valid indicator of the presence of residues due to its fast degradation, the residue definition was established as clodinafop. The EPCO experts' meeting (EPCO 19) recommended inclusion of its S isomer in the residue definition. This inclusion needs to be decided at risk management level as there is no data demonstrating the actual occurrence of the S-isomer in plants and as no information is available on its intrinsic toxicological properties.

In animal metabolism, clodinafop was identified as major metabolite in all edible organs and tissues of ruminants and poultry.

Supervised residue trials demonstrated the absence of residues above the analytical LOQ (It should be noted that the method of analysis used in the residue trials is not isomer specific and consequently measures the sum of both isomers if they are both present). The MRL may be established at 0.02* mg/kg for wheat, rye and triticale. In succeeding and rotational crops, no residues are expected and no crop or cultivation restrictions are necessary.

Chronic and acute exposures of consumers to residues resulting from the use of clodinafop propargyl are far below the ADI and the ARfD respectively, indicating the absence of a dietary risk.

First degradation step of clodinafop-propargyl in soil yields clodinafop that is further degraded. Only metabolite CGA 302371 was detected in amounts above the 10 % AR. Unextractable residues evolved to a maximum of about 58 % AR. CO_2 evolved to maximums between 33- 60 % AR. Under anaerobic conditions no new metabolites were identified. Degradation in natural soils proceeds mainly through enzymatic / microbial processes.

Photolysis does not contribute to the degradation of clodinafop-propargyl in soil but may contribute to the degradation of clodinafop.

Clodinafop-propargyl may be considered to be low or very low persistent in soil. The formed clodinafop is low to moderate persistent in soil ($DT_{50\ 20\ °C\ lab}$ = 7.4 – 18 d) and its metabolite CGA 302371 is low persistent in soil ($DT_{50\ 20\ °C\ lab}$ = 8.8 – 12 d).

Results of field dissipation studies confirm the low persistence of clodinafop-propargyl, clodinafop and metabolite CGA 302371. The persistence criteria laid down in Annex VI of 91/414/EEC are fulfilled.

PEC soil for clodinafop-propargyl, clodinafop and CGA 302371 were calculated by the RMS.

Clodinafop–propargyl may be classified as medium to low mobile in soil, clodinafop and metabolite CGA 302371 may be classified as very high mobile. Minor metabolite CGA 193468 may be classified as medium mobile in soil. No relationship was observed between soil pH and adsorption of clodinafop.

Clodinafop-propargyl was instable at all the pH tested. The major hydrolysis product was clodinafop that was hydrolytically stable. The hydrolytic half life of CGA 302371 at ambient temperature may be estimated to be > 1 year.

Photolysis in water produces clodinafop as main product. Clodinafop was in turn broken down to yield CGA-193468 (maximum of 6.3%). Photolysis may contribute to the environmental degradation

of clodinafop-propargyl and clodinafop in water. No new major photodegradation products have been identified.
Clodinafop-propargyl is not readily biodegradable.
In the water / sediment studies the parent compound was quantitatively converted into clodinafop in less than one day. Clodinafop degraded in the whole system with DT_{50} values of 72 d at 20 °C. The main degradation product was CGA 302371 (DT_{50} = 142 or > 68 d at 20 °C). Metabolite CGA 193468 was found at amounts up to 10 % AR in the sediment (DT_{50} > 68 d). The pathway of degradation was similar under anaerobic conditions but at slower rate. The lifetime of CGA 302371 in natural aquatic systems is likely to be controlled by photochemical degradation.
PECsw and PECsed estimations were based drift as the entry route to surface water.
Predicted 80th percentile annual leachate concentrations of clodinafop-propargyl, clodinafop and metabolite CGA 302371 were below 0.1 µg / L trigger for all compounds and situations modelled with FOCUS-PEARL.
Concentrations of Clodinafop-propargyl clodinafop and its metabolites in air are likely to be negligible.

Due to the fact that no enantioselective analysis was performed during the fate and behaviour studies, racemization in the different environmental compartments may not be excluded. Therefore, S isomers of clodinafop-propargyl and clodinafop are included in the residue definition.
In case that isomerization takes place it is assumed that the S-isomers are also formed in the ecotoxicological tests and that the endpoints deriving from the tests would cover the toxicity of the potentially formed S-isomer.

The risk to birds and mammals, aquatic organisms, bees, other non-target arthropods and earthworms from the representative use of Topik 100 EC was assessed to be low.
An effect of > 25 % on soil micro-organisms was observed in a soil microbial nitrogen transformation test with the soil metabolite CGA 302371. Taking into account that CGA 302371 was formed during the test with clodinafop-propargyl (in the sandy loam soil, the same soil as was used in the soil micro-organism study, the maximum of 18.3 % was reached at 0.1 days) and that the initial PEC soil of CGA 302371 is a factor 367 lower than the treatment rate in the study with the parent where no effects > 25 % were observed, it is considered as unlikely that CGA 302371 would pose a high risk to soil micro-organisms. In order to support this assumption with data a new study with the metabolite CGA 302371 is proposed as a confirmatory data requirement. A new study with the metabolite CGA 302371 and soil micro-organisms was conducted by the notifier (W. Voelkl (2005). The study was not assessed and not peer reviewed.
The risk to non-target plants is considered to be low if a buffer zone of 1 m to off-field non target plants is applied.

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

- None

Critical areas of concern

- No enantio selective analytical method is available for the determination of residue in food of plant origin (the necessity depends on the final residue definition).
- The potential of stereochemical inversion of the R-isomer into to S-isomer in plant metabolism has not been addressed. In case this stereochemical inversion occurs in practice, it is not sure that the toxicological end points set for the active substance cover adequately the effects of residues the consumer are actually exposed to.

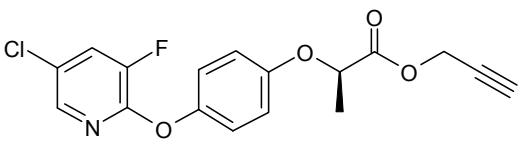
APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

(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) ‡	Clodinafop (ISO) (unless otherwise stated, the following data relate to the variant clodinafop-propargyl)
Function (e.g. fungicide)	Herbicide
Rapporteur Member State	The Netherlands
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	Prop-2-ynyl (*R*)-2-[4-(5-chloro-3-fluoro-pyridin-2-yloxy)-phenoxy]-propionionate
Chemical name (CA) ‡	(*R*)-2-[4-[(5-chloro-3-fluoro-2-pyridinyl)oxy]phenoxy]-propanoic acid 2-propynyl ester
CIPAC No ‡	683.225
CAS No ‡	105512-06-9
EEC No (EINECS or ELINCS) ‡	Not available
FAO Specification ‡ (including year of publication)	No FAO specification available
Minimum purity of the active substance as manufactured ‡ (g/kg)	950 g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	none
Molecular formula ‡	$C_{17}H_{13}ClFNO_4$
Molecular mass ‡	349.8
Structural formula ‡	

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

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity)	59.5 °C (995 g/kg)
Boiling point (state purity)	Thermal decomposition starts at about 285 °C 100.6 °C at 0.082 Pa (999 g/kg)
Temperature of decomposition	Thermal decomposition starts at about 285 °C
Appearance (state purity)	White crystalline powder (995 g/kg) Light beige powder (973 g/kg)
Relative density (state purity)	Density: 1.35 g/cm^3 (999 g/kg)
Surface tension	σ = 72.3 mN/m at 20 °C and 90% saturation concentration
Vapour pressure (in Pa, state temperature)	$3.19 \cdot 10^{-6}$ Pa at 25 °C
Henry's law constant (Pa m^3 mol $^{-1}$)	$2.8 \cdot 10^{-4}$ Pa · m³ / mol
Solubility in water (g/l or mg/l, state temperature)	4.0 mg/l at 25 °C
Solubility in organic solvents (in g/l or mg/l, state temperature)	At 25 °C: acetone > 500 g/l dichloromethane > 500 g/l ethyl acetate > 500 g/l hexane 7.5 g/l methanol 180 g/l octanol 21 g/l toluene > 500 g/l
Partition co-efficient (log P_{OW}) (state pH and temperature)	log P_{ow} = 3.90 ± (0.15) at 25 °C in pure water No pH effect as there is no dissociation Clodinafop (CGA 193469): log P_{ow} = -0.44 at 25 °C and pH 6.9 (neutral+ionized) log P_{ow} = 3.5 at 25 °C and pH 6.9 (neutral species) CGA 193468: log P_{ow} = 3.0 at 25 °C and pH 7 CGA 302371: log P_{ow} = 0.52 at 25 °C and pH 7.0
Hydrolytic stability (DT_{50}) (state pH and temperature)	pH 4 $t_{0.5}$ = 17.9 days at 25 °C pH 5 $t_{0.5}$ = 26.8 days at 25 °C pH 7 $t_{0.5}$ = 4.8 days at 25 °C pH 9 $t_{0.5}$ = 0.07 days at 25 °C
Dissociation constant	No dissociation constant within the range 2 to 12

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UV/VIS absorption (max.) (if absorption > 290 nm state Σ at wavelength)	Molar extinction coefficients: neutral at 226 nm 15982 l/mol · cm at 279 nm 4910 l/mol · cm at 290 nm 3550 l/mol · cm acidic at 226 nm 18988 l/mol · cm at 279 nm 6382 l/mol · cm basic at 227 nm 19045 l/mol · cm at 280 nm 6745 l/mol · cm
Photostability (DT_{50}) (aqueous, sunlight, state pH)	At pH 5 and 25 °C the DT_{50} was determined as 24.23 days using a xenon lamp with intensity adjusted to natural sunlight. Only one degradation product was formed > 10%: CGA 193469.
Quantum yield of direct photo transformation in water at Σ > 290 nm	Φ = 0.0237
Flammability	Clodinafop-propargyl is not considered highly flammable
Explosive properties	Clodinafop-propargyl is not considered an explosive

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

List of representative uses evaluated*

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					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 as/hl min max	water l/ha min max	kg as/ha min max		
wheat, rye and triticale	Northern MS	TOPIK	F	post-emergent grass herbicide	100 EC	100 g/L		GS 39 Spring	1	--	0.015 – 0.06	100 - 400	max: 0.06		-
wheat, rye and triticale	Southern MS	TOPIK	F	post-emergent grass herbicide	100 EC	100 g/L		GS 39 Spring	1	--	0.015 – 0.06	100 - 600	max: 0.06		-

Remarks:	*	Uses for which risk assessment could not been concluded due to lack of essential data are marked grey	(h)	Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
	(a)	For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)	(i)	g/kg or g/L
	(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)	(k)	The minimum and maximum number of application possible under practical conditions of use must be provided
	(e)	GCPF Codes - GIFAP Technical Monograph No 2, 1989		
	(f)	Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench	(l)	PHI - minimum pre-harvest interval
	(g)	All abbreviations used must be explained	(m)	Remarks may include: Extent of use/economic importance/restrictions

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Appendix 1.2: Methods of Analysis

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

Technical as (principle of method)	GC and HPLC for enantiomer separation
Impurities in technical as (principle of method)	GC
Plant protection product (principle of method)	GC

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	The method is not enantio selective. Wheat grain, straw and whole green plant were extracted with hexane:diethyl ether extraction, reconstituted in phosphate buffer pH 7, extracted against hexane followed by C-18 SPE and reconstitution in ion pair reagens solution. Detection was HPLC with UV-detection (single column). LOQ: 0.02 ppm (grain), 0.05 ppm (straw and whole green plant, clodinafop (CGA 193469)). For confirmation an LC/MS/MS method can be used (extraction with acetone/citrate buffer followed by SPE clean-up, both C18 and ENVI-Carb. Determination with RP-HPLC-MS/MS). Used for clodinafop-propargyl and clodinafop (CGA 193469).
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	The method is not enantio selective. Analytical methods for the determination of residues of clodinafop-propargyl in food/feedstuff of animal origin are not required since no residue definition is proposed. Still, a method was developed (suited for pre-registration purposes only). The method is not enantio selective: Beef meat, fat, liver and milk and chicken meat and eggs samples were extracted with hexane:diethyl ether, reconstituted in phosphate buffer pH7:concentrated NaCl solution, extracted against hexane (beef liver and fat only) followed by C-18 SPE and reconstitution in methanol:water:trifluoroacetic acid. Determination was HPLC with UV-detection (two-column-switching). Beef fat was heated for extraction. LOQ: 0.02 mg/kg (clodinafop-propargyl, all commodities).
Soil (principle of method and LOQ)	The method is not enantio selective. Extraction with acetone-buffer pH 7 and acetone-

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	5% formic acid. After evaporation of acetone and addition of water and 1% formic acid, the extract is cleaned up using a C18 (metabolite CGA 302371) or a C8 SPE cartridge (Clodinafop-propargyl and clodinafop (CGA 193469)) and analysed by LC/MS/MS. LOQ: 0.005 mg/kg (clodinafop-propargyl, CGA 302371 and clodinafop (CGA 193469)
Water (principle of method and LOQ)	The method is not enantio selective. Clodinafop-propargyl and clodinafop (CGA 193469): Addition of acetic acid, SPE extraction, analysis by HPLC-MS/MS LOQ (drinking-, ground- and surface water) 0.05 µg/L CGA 302371: SPE extraction, analysis with LC-MS/MS; LOQ: 0.1 µg/L (drinking-, ground- and surface water)
Air (principle of method and LOQ)	No acceptable methods available. (submitted in the meantime, but not evaluated)
Body fluids and tissues (principle of method and LOQ)	Not required (not classified as T or T+)

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	none

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

Appendix 1.3: Impact on Human and Animal Health

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

Rate and extent of absorption ‡	75% based on radiolabel recovered in urine, tissues, cage wash and residual carcass within 168 h in males only. Higher oral absorption in females.
Distribution ‡	Widely; highest residues in fat, muscle, liver, blood and kidneys. Residues higher in males than females.
Potential for accumulation ‡	Potential accumulation in fat. Elimination was slow from ovaries, pancreas, thymus and thyroid.
Rate and extent of excretion ‡	Urinary (24 h): 16-27% (m), 77-87% (f) Faecal (24 h) 7-9% (m), 2-5% (f) Total excretion (7d) : 66-85% (m), 92-96% (f)
Metabolism in animals ‡	Extensively metabolised, <0.3% remaining as parent.
Toxicologically significant compounds ‡ (animals, plants and environment)	Clodinafop-propargyl (and its S- isomer)

Acute toxicity (Annex IIA, point 5.2)

Rat LD50 oral ‡	1392 mg/kg bw (m) 2271 mg/kg bw (f)	R22
Rat LD50 dermal ‡	> 2000 mg/kg bw	
Rat LC50 inhalation ‡	> 2.3 mg/L air (4h)	
Skin irritation ‡	Non-irritating	
Eye irritation ‡	Non-irritating	
Skin sensitization ‡ (test method used and result)	Sensitising (Optimisation study)	R43

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver and haematological parameters (rats and dogs). Thymic atrophy observed at high dose levels
Lowest relevant oral NOAEL / NOEL ‡	3.4 mg/kg bw/day, 1 year dog
Lowest relevant dermal NOAEL / NOEL ‡	50 mg/kg bw/day, 4 weeks rat
Lowest relevant inhalation NOAEL / NOEL ‡	No data – not required

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

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	No genotoxic potential

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

Target/critical effect ‡	Liver (rat and mouse) and haematological (rat) parameters, peroxisome proliferation (rat and mouse).
Lowest relevant NOAEL / NOEL ‡	0.32 mg/kg bw/day, 2 year rat
Carcinogenicity ‡	Rats and mice: benign and malignant hepatomas at highest dose level. Irrelevant to human risk assessment (species specific effect).

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	No specific reproductive effect.	
Lowest relevant reproductive NOAEL / NOEL ‡	Reproduction: ≥ 89 mg/kg bw/day Parental: 4.63 mg/kg bw/day	
Developmental target / critical effect ‡	Delayed or absent ossification and increase in genito-urinary tract variations at doses producing effects in other general toxicity studies (rat)	
Lowest relevant developmental NOAEL / NOEL ‡	Maternal: 160 mg/kg bw/day Developmental: 5 mg/kg bw/day	R63?

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

.....	No data, no concern from other studies, no study required.

Other toxicological studies ‡ (Annex IIA, point 5.8)

.....	Liver peroxisome proliferation demonstrated in rats and mice. *In vitro* investigations with human hepatocytes demonstrated lack of relevance to human risk assessment.

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

Medical data ‡ (Annex IIA, point 5.9)

.....	Four incidental cases of health effects to workers in manufacturing plants have been reported between 1994 and 2001: chemical burn on skin, feeling of empty head and sleepiness, and stinging in the eyes. No evidence of adverse effects to agricultural workers.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.003 mg/kg bw/day	2-year rat, oral	100
AOEL ‡	0.026 mg/kg bw/day	1-year, dog, oral	133*
ARfD ‡ (acute reference dose)	0.05 mg/kg bw	2-generation reproduction and dev tox in rat	100

* Correction for low oral absorption, 75% (males)

Dermal absorption (Annex IIIA, point 7.3)

Topik 100 EC (10% EC)	2.5% (concentrated formulation); 10% (diluted formulation); derived from rat *in vivo* data modified by comparative rat: human *in vitro* data.

Acceptable exposure scenarios (including method of calculation)

Operator	Estimated exposure (% of AOEL) based on the UK POEM and German model without PPE, application rate 0.06 kg a.i./ha. UK POEM 80% German model 20%
Workers	Based on the use of Topic 100 EC as herbicide in small cereal grains, no intensive contact with the crop is anticipated after application and therefore a worker re-entry risk assessment is not considered necessary.
Bystanders	The estimated bystander exposure is below the AOEL for proposed uses of Topic 100 EC without any PPE according to EUROPOEM II (<1%).

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

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	Xn	Harmful
	R22	Harmful if swallowed
	R43	May cause sensitization by skin contact

‡ 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	Cereals (wheat grain)
Rotational crops	Lettuce, sugar beet, winter wheat, maize, mustard and turnip
Plant residue definition for monitoring	Clodinafop or sum of clodinafop and its S isomer expressed as clodinafop (cereals only)
Plant residue definition for risk assessment	Clodinafop or sum of clodinafop and its S isomer expressed as clodinafop (cereals only)
Conversion factor (monitoring to risk assessment)	1

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

Animals covered	Goat, hen.
Animal residue definition for monitoring	Not applicable. (no significant residues in livestock diet and no accumulation of residues in edible animal products expected)
Animal residue definition for risk assessment	Not applicable. (no significant residues in livestock diet and no accumulation of residues in edible animal products expected)
Conversion factor (monitoring to risk assessment)	Not applicable
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes (Log P_{OW} of clodinafop is 3.5 at Ph 6.9, 25 °C).

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

.....	Total radioactive residue (TRR): Plantback interv. 30-270 d: mature wheat: = 0.004 mg eq/kg Straw = 0.018 mg eq/kg Plantback interv. 30-92 d: turnip leaves: = 0.006 mg eq/kg tubers: < 0.003 mg eq/kg Plantback interv. 30-92 d: mustard leaves: = 0.006 mg eq/kg Plantback interv. 82-98 d: lettuce: < 0.001 mg eq/kg

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

	Plantback interv. 82-379 d: sugar beet: < 0.001 mg eq/kg Plantback interv. 30-379 d: corn: < 0.001 mg eq/kg

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

.....	clodinafop is stable in wheat grain and straw stored at -18°C for at least two years

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

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	Yes (beef cattle: 0.0055 mg/kg bw, corresponding to 0.13 mg/kg dry feed; dairy cattle: 0.002 mg/kg bw, corresponding to 0.06 mg/kg dry feed)	No	No
Potential for accumulation (yes/no):	No	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No	No	No
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	Not required	Not required	Not required
Liver	Not required	Not required	Not required
Kidney	Not required	Not required	Not required
Fat	Not required	Not required	Not required
Milk	Not required		
Eggs		Not required	

‡ 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 representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Wheat grain	NMS	8 x <0.02, 8 x <0.05, 6 x <0.1	LOQ is 0.02 mg/kg	0.02*	<0.02	<0.02
Wheat grain	SMS	7 x 0.02		0.02*	<0.02	<0.02
Wheat straw	NMS	0.013, <0.05, 0.06, 0.065, 0.08, 2 x 0.095, 0.10, 0.12, 0.14, 0.16, 0.17			0.17	0.095
Wheat straw	SMS	4 x <0.05, 3 x <0.1			<0.1	<0.05

(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	0.003 mg/kg bw/day
ITMDI (European Diet) (% ADI)	0.0037 mg/person/day (1.9% of the ADI)
NTMDI (Dutch diet) (% ADI)	0.0027 mg/person/day (1.3% of the ADI) 0.0017 mg/child (1-6 y)/day (3.1% of the ADI)
ARfD	0.05 mg/kg bw/day
Acute exposure (% ARfD)	0.0063 mg/person/day (0.2% of the ARfD) 0.0035 mg/child (1-6 y)/day (0.4% of the ARfD)

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

Crop/processed crop	Number of studies	Transfer factor	% Transference*
Not applicable	-	- [1]	- [1]

[1] No measurable residues are likely to be found in raw agricultural commodity and the calculated TMDI is <10% of the ADI. Hence, processing studies are not required.
* 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)

.....	Wheat grain: 0.02* mg/kg Rye grain: 0.02* mg/kg Triticale grain: 0.02* mg/kg

*) LOQ

‡ 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 ‡	35.2-41.9% AR after 84 d (phenyl-label, 1 soil) 23.4-29.4% AR after 84 d (pyridinyl-label, 4 soils)
Non-extractable residues after 100 days ‡	52.2-53.7% AR after 84 d (phenyl-label, 1 soil) 47.8-58.2% AR after 84 d (pyridinyl-label, 4 soils)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	**Clodinafop (CGA 193469)** 67.5– 95.2% AR after 0.1 – 7 d **CGA 302371** 8.8 – 18.3% AR after 0.1 – 56 d

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

Anaerobic degradation ‡	Anaerobic flooded soil: rate of degradation of clodinafop-propargyl similar to that in aerobic soil, only metabolite detected clodinafop (CGA 193469, max. 98.1% on day 1) stable; limited formation of CO2 and bound residues (max. 0.18 and 3.9% AR, respectively, after 120 days).
Soil photolysis ‡	DT_{50}: **Clodinafop-propargyl** Viable soil: insignificant effect of irradiation on rate of degradation **Clodinafop** (CGA 193469) Viable soil: rate of degradation enhanced by irradiation (DT50 under test conditions (Xenon light) 35 hours, corresponding with an environmental photolysis half-life at 30°N and 50°N of 8.6 and 9.0 days, respectively).
Field dissipation	**Four German trials**(A): residues of Clodinafop-propargyl at or below the quantifiable limit (=0.01 mg/kg) in samples taken on the day of application and at all later dates after a dose of 0.4 kg a.s./ha applied in May. Metabolites: CGA 193469 and CGA 302371. **UK field monitoring study**(A), 2 locations (sand and clay soil), treatment of winter wheat in December, dose 60 g a.s./ha: Clodinafop-propargyl not detectable (<0.005 mg/kg) at sand site, only detected on day of application at 0.003 mg/kg at clay site. Metabolites: clodinafop (CGA 193469) and CGA 302371.

(A) Provisional data (additional information on study requested)

‡ 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	Graphical or first-order kinetics (**Clodinafop-propargyl**), first-order kinetics (**Clodinafop** (CGA 193469), **CGA 302371**)
Laboratory studies (range or median, with n value, with r^2 value)	DT_{50}, lab (20◦C, aerobic): **Clodinafop-propargyl** (4 soils) <0.1 d (graphical) 1.5 d (1st order, r2 1.00) 0.8 d (1st order, r2 1.00) 0.7 d (1st order, r2 1.00) average DT50 value: 0.8 d **Clodinafop** (CGA 193469) (4 soils) 7.4 d (1st order, r2 0.95-1.00; mean of 3 experim.) 18 d (1st order, r2 0.99) 11 d (1st order, r2 0.97) 13 d (1st order, r2 0.98) average DT50 value: 12 d **CGA 302371** (3 soils) 8.8 d (1st order, r2 0.99) 9.4 d (1st order, r2 0.99) 12 d (1st order, r2 0.98) average DT50 value: 10 d
	DT_{90}, lab (20◦C, aerobic): Graphical or first-order kinetics estimation (Clodinafop-propargyl), first-order kinetics estimation (Clodinafop (CGA 193469), CGA 302371) **Clodinafop-propargyl** <0.1, 4.9, 2.6 and 2.4 days, mean 2.5 d (n=4) **Clodinafop** (CGA 193469) 24, 61, 37 and 42 days, mean 41 d (n=4) **CGA 302371** 29, 31 and 41 days, mean 34 d (n=3)
	$DT_{50, lab}$ (10◦C, aerobic): calculated from $DT_{50, lab}$ (20◦C, aerobic) using a Q_{10} factor of 2.2 **Clodinafop-propargyl** (4 soils) <0.2 d 3.3 d 1.8 d 1.6 d average DT_{50} value: 1.7 d

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	Clodinafop (CGA 193469) (4 soils) 17 d 40 d 24 d 29 d average DT_{50} value: 28 d **CGA 302371** (3 soils) 20 d 21 d 27 d average DT_{50} value: 22 d
	$DT_{50, lab}$ (20°C, anaerobic flooded, 1 soil): Clodinafop-propargyl: 0.1 day **Clodinafop** (CGA 193469): stable
	degradation in the saturated zone: not available and not required
Field studies (state location, range or median with n value)	**Four German trials**, dose of 0.4 kg a.s./ha applied in May: **Clodinafop-propargyl** residues at or below the quantifiable limit (=0.01 mg/kg) in samples taken on the day of application and at all later dates. **Clodinafop** (CGA 193469): DT50 (field) 13, 4.6, 7.7 and 6.6 d, mean 8.0 d DT90 (field) 43, 15, 26 and 22 d, mean 27 d **CGA 302371**: max. 0.005 mg/kg **UK field study**, 2 locations (sand and clay soil), treatment of winter wheat in December, dose 60 g a.s./ha. **Clodinafop-propargyl** not detectable (<0.005 mg/kg) at sand site, only detected on day of application at 0.003 mg/kg at clay site. **Clodinafop** (CGA 193469): DT50 (field) 19 and 33 d; DT90 (field) 63 and 108 d **CGA 302371**: max. 0.007 and 0.009 mg/kg after 90 days at sand and clay site respectively

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

Soil accumulation and plateau concentration	**Field residue trial**, Switzerland, dose of 0.1 kg a.s./ha applied in May to wheat: **Clodinafop-propargyl** and **Clodinafop** (CGA 193469) residues below the quantifiable limit (<0.1 mg/kg) in samples taken on the day of application and at all later dates up to day 516. Four year **field accumulation trial**, Switzerland, dose of 0.1 kg a.s./ha (1st 3 years) or 0.06 kg a.s./ha (4th year) applied in May to cropped soil: During the first year, residues of **Clodinafop-propargyl** and **Clodinafop** (CGA 193469) were below the quantifiable limit (<0.1 mg/kg) in samples up to day 180 after treatment. Residues of Clodinafop-propargyl and Clodinafop (CGA 193469)were also below the quantifiable limit in samples taken just before and 71-112 days after treatment during the second year (<0.02 and <0.1 mg/kg respectively) and the third and fourth year (<0.01 mg/kg).

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence ‡ (yes / no) (if yes type of dependence)	K_F, Koc and 1/n values are listed in corresponding order of soils **Clodinafop-propargyl** K_F values: 2.4, 12.8, 16.6, 99.3 and 311 L/kg (average 88.4 L/kg) 1/n: 0.86, 1.04, 0.80, 0.94 and 0.96 (average 0.92) Koc values: 252, 1829, 1195, 2364 and 1588 L/kg (average 1446 L/kg) no pH dependence **Clodinafop** (CGA 193469) (4 soils) K_F values: 1.11, 0.50, 1.06, 1.00 and 0.80 L/kg (average 0.89 L/kg) 1/n: 0.95, 0.99, 0.81, -$^{(A)}$ and -$^{(A)}$ (average 0.92) Koc values: 25.3, 65.8, 50.5, 37.0 and 52.9 L/kg (average 46.3 L/kg) no pH dependence **CGA 302371** K_F values: 1.1, 0.62 and 0.89 L/kg (average 0.87 L/kg) 1/n: 0.96, 0.84 and 0.89 (average 0.90) Koc values: 25.1, 81.6 and 42.4 L/kg (average 49.7 L/kg) pH dependence not established (soil pH 7.0-7.3;

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	above Koc values are acceptable worst case values with respect to pH) **CGA 193468** K_F values: 4.3, 5.4 and 4.0 L/kg (average 4.6 L/kg) 1/n: 0.79, 0.82 and 0.73 (average 0.78) Koc values: 238, 365 and 253 L/kg (average 285 L/kg) pH dependent (higher sorption at lower pH in 3 soils of pH 4.2, 7.3 and 7.5)

(A) No Freundlich coefficient determined.

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

Column leaching ‡	no reliable data available and not required
Aged residues leaching ‡	biologically aged for 28 d, two soils, leached for 16 d with total of 200 mm water In 28-day aged soil: Clodinafop-propargyl (0.44-0.81% AR), CGA 193469 (not detectable - 0.96% AR), unidentifieds (4.52-10.6% AR), non-extractable (48.9-63.2% AR), CO_2 (25.1-41.8% AR). In eluted soil column: Total RA 55.0-65.3% AR (45.4-64.2% AR in top 4 cm); Clodinafop-propargyl and CGA 193469 not detectable (<0.05% AR). In leachate: Total RA 0.03-0.60% AR (not further analysed).
Lysimeter/ field leaching studie ‡	UK field study, 2 locations (sand and clay soil), treatment of winter wheat in December, dose 60 g a.s./ha. Clodinafop-propargyl and clodinafop (CGA 193469) not detected (<0.05 µg/L) in groundwater at 25, 50 and 80-120 cm depth.

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

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	**Clodinafop-propargyl**: 50% crop interception 5 cm soil incorporation soil density 1.5 g/cm^3 DT_{50} used: 1.5 d (worst case) Metabolites: highest percentage of formation, correction for molar mass ratio (MMR), worst case DT50 (lab) **Clodinafop** (CGA 193469) DT_{50} 18 d (worst case); max. % = 95.2; MMR = 311.7/349.8 **CGA 302371** DT_{50} 12 d (worst case); max. % = 18.3; MMR = 147.4/349.8
Application rate	single treatment to cereals at 0.06 kg as/ha

day after	Clodinafop-propargyl		Clodinafop (CGA 193469)		CGA 302371	
appln.	actual	TWA	actual	TWA	actual	TWA
0	0.040	0.040	0.034	0.034	0.003	0.003
1	0.025	0.032	0.033	0.033	0.003	0.003
2	0.016	0.026	0.031	0.033	0.003	0.003
4	0.006	0.018	0.029	0.031	0.002	0.003
7	0.002	0.012	0.026	0.030	0.002	0.003
21	2E-06	0.004	0.015	0.023	0.001	0.002
28	1E-07	0.003	0.012	0.021	0.001	0.002
50	4E-12	0.002	0.005	0.015	2E-04	0.001
100	3E-22	0.001	0.001	0.009	1E-05	0.001

‡ 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)	**Clodinafop-propargyl** pH 4, 25°C: DT_{50} 17.9 d pH 5, 25°C: DT_{50} 26.8 d pH 7, 25°C: DT_{50} 4.8 d pH 9, 25°C: DT_{50} 0.07 d Major hydrolysis product: **Clodinafop** (CGA 193469) (max. 99.3% AR) hydrolytically stable **CGA 193468** pH 4, 7, and 8.8 at 50°C: hydrolytically stable **CGA 302371** pH 4, 7, and 8.8 at 50°C: hydrolytically stable
Photolytic degradation of active substance and relevant metabolites ‡	**Clodinafop-propargyl** buffer pH 5/acetonitrile, 25°C, mercury light >290 nm: DT_{50} under test conditions 20.4 d (^{14}C-phenyl label) and 24.2 d (^{14}C-pyridinyl label). CGA 193469: max: 12.7% after 15 days. (Also in water/sediment system). No other individual metabolite > 6.5%. Buffer pH 7/acetonitrile (1/1), 20°C, monochromatic mercury light (280 nm): quantum yield 0.0211. Calculated environmental photolysis half-lives in water: 5.8 d (spring, 40°N) 9.5 d (spring, 50°N) 4.0 d (summer, 40°N) 4.8 d (summer, 50°N)
	Clodinafop (CGA 193469) buffer pH 7 with 1% acetonitrile, 20°C, monochromatic xenon light (279 nm): quantum yield 0.00782. Calculated environmental photolysis half-lives in water: 8.5 d (spring, 40°N) 12.5 d (spring, 50°N) 6.0 d (summer, 40°N) 7.0 d (summer, 50°N) **CGA 193468** buffer pH 5.2, 7.1 and 9.0 with <1% acetonitrile, 20°C, polychromatic xenon light (>290 nm): quantum yield 5.73E-04, 8.35E-04 and 5.58E-04 at pH 5.2, 7.1 and 9.0 respectively. Calculated minimum environmental photolysis half-lives at 40°N and 50°N 58 and 73 days (pH 7.1, summer) and maximum half-lives 197 and 321 days (spring, pH 5.2).

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

	CGA 302371 buffer pH 5.2, 7.1 and 9.1 with <1% acetonitrile, 20°C, polychromatic xenon light (>290 nm): quantum yield 0.028, 0.033 and 0.198 at pH 5.2, 7.1 and 9.1 respectively. Calculated minimum and maximum environmental photolysis half-lives, respectively, at 40°N and 50°N during spring and summer 12-14 and 64-81 min.
Readily biodegradable (yes/no)	no (26% biodegradation after 29 days)
Degradation in water/sediment	**Aerobic** study (2 systems), 20°C ([A] Range for incubation with phenyl- and pyridinyl-labeled test compound): **Clodinafop-propargyl** $DT_{50, water}$: 0.2 d (r^2 -) and 0.1 d (r^2 -) [1st order] $DT_{50, sediment}$: 0.3 d (r^2 -) and 0.1-0.2 d[A] (r^2 -) [1st order] $DT_{50, system}$: 0.2 d (r^2 -) and 0.1 d (r^2 -) [1st order] **Clodinafop** (CGA 193469) $DT_{50, water}$: 68 d (r^2 -) and 29-30[A] d (r^2 -) [1st order] $DT_{50, sediment}$: 65 d (r^2 0.89) and 6.3-6.4[A] d (r^2 -) [1st order] $DT_{50, system}$: 72 d (r^2 -) and 38 d (r^2 -) [graphically] **CGA 302371** $DT_{50, water}$: 134 d (r^2 -) [1st order] and >68 d (r^2 -) [graphically] $DT_{50, sediment}$: 165 d (r^2 -) [1st order] and >68 d (r^2 -) [graphically] $DT_{50, system}$: 142 d (r^2 -) [1st order] and >68 d (r^2 -) [graphically] **Aerobic** study (1 system), 9°C: **Clodinafop-propargyl** Not detectable at first sampling (day 7) **Clodinafop** (CGA 193469) $DT_{50, water}$: 98 d (r^2-) – 40.6 d at 20°C [1st order] $DT_{50, sediment}$: 81 d (r^2-)– 33.6 d at 20°C [1st order] $DT_{50, system}$: 107 d (r^2-)– 44.4 d at 20°C [1st order] **CGA 302371** $DT_{50, water}$: >175 d (r^2-) – > 72.6 d at 20°C [1st order] $DT_{50, sediment}$: >175 d (r^2-)– > 72.6 d at 20°C [1st order] $DT_{50, system}$: >175 d (r^2-)– > 72.6 d at 20°C [1st order] **Average values** (Range for incubation with phenyl- and pyridinyl-labeled test compound averaged) **Clodinafop-propargyl**

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

$DT_{50, water}$: 0.2 d (n=2; 0.2 and 0.1 d) $DT_{50, sediment}$: 0.2 d (n=2; 0.3 and 0.15 d) $DT_{50, system}$: 0.2 d (n=2; 0.2 and 0.1 d) **Clodinafop** (CGA 193469) $DT_{50, water}$: 46 d (n=3; 68, 29.5 and 40.6 d) $DT_{50, sediment}$: 35 d (n=3; 65, 6.35 and 33.6 d) $DT_{50, system}$: 51 d (n=3; 72, 38 and 44.4 d) **CGA 302371 (median values)** $DT_{50, water}$: 73 d (n=3; 134, >68 and >72.6 d) $DT_{50, sediment}$: 73 d (n=3; 165, >68 and >72.6 d) $DT_{50, system}$: 73 d (n=3; 142, >68 and >72.6 d)
Anaerobic study (1 system), 20°C: **Clodinafop-propargyl** Not detectable at first sampling (day 28) **Clodinafop** (CGA 193469) $DT_{50, water}$: >217 d (r^2 -) [graphically] $DT_{50, sediment}$: >217 d (r^2 -) [graphically] $DT_{50, system}$: >217 d (r^2 -) [graphically]
DT90 extrapolated from DT_{50} values as $3.3 \cdot DT_{50}$, assuming first order exponential decay, or determined graphically (by inter- or extrapolation)
Aerobic study (2 systems), 20°C ($^{(A)}$ Range for incubation with phenyl- and pyridinyl-labeled test compound): **Clodinafop-propargyl** $DT_{90, water}$: 0.6 d (r^2 -) and 0.3 d (r^2 -) $DT_{90, sediment}$: 0.9 d (r^2 -) and 0.5-0.6 d$^{(A)}$ (r^2 -) $DT_{90, system}$: 0.8 d (r^2 -) and 0.3 d (r^2 -) **Clodinafop** (CGA 193469) $DT_{90, water}$: 85 d (r^2 -) and 51-52$^{(A)}$ d (r^2 -) $DT_{90, sediment}$: 217 d (r^2 0.89) and 21 d (r^2 -) $DT_{90, system}$: 88 d (r^2 -) and 53-54$^{(A)}$ d (r^2 -) **CGA 302371** $DT_{90, water}$: 444 d (r^2 -) and >68 d (r^2 -) $DT_{90, sediment}$: 548 d (r^2 -) and >68 d (r^2 -) $DT_{90, system}$: 471 d (r^2 -) and >68 d (r^2 -)

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

	Aerobic study (1 system), 9°C: **Clodinafop-propargyl** Not detectable at first sampling (day 7) **Clodinafop** (CGA 193469) $DT_{90, water}$: 154 d (r^2 -) $DT_{90, sediment}$: >294 d (r^2 -) $DT_{90, system}$: 150 d (r^2 -) **CGA 302371** $DT_{90, water}$: >175 d (r^2 -) $DT_{90, sediment}$: >175 d (r^2 -) $DT_{90, system}$: >175 d (r^2 -)
	Anaerobic study (1 system), 20°C: **Clodinafop-propargyl** Not detectable at first sampling (day 28) **Clodinafop** (CGA 193469) $DT_{90, water}$: >217 d (r^2 -) $DT_{90, sediment}$: >217 d (r^2 -) $DT_{90, system}$: >217 d (r^2 -)
Mineralization	**Aerobic** studies, 20°C: 14C-pyridinyl Clodinafop-propargyl (1st system): 4.3% after 91 d, 19.7% after 259 d (end) 14C-pyridinyl Clodinafop-propargyl (2nd system): 23.8-31.2% after 91-126 d 14C-phenyl Clodinafop-propargyl (2nd system): 39.1-40.7% after 91-126 d **Aerobic** study, 1 system, 9°C: 14C-pyridinyl Clodinafop-propargyl: 1.9% after 91 d, 19.5% after 357 d (end) **Anaerobic** study, 1 system, 20°C: 14C-pyridinyl Clodinafop-propargyl: 0.5% after 91 d, 1.9% after 245 d (end)

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

Non-extractable residues	**Aerobic** studies, 20°C: 14C-pyridinyl Clodinafop-propargyl (1st system): 31.4% after 91 d, 43.2% after 259 d (end) 14C-pyridinyl Clodinafop-propargyl (2nd system): 35.2% after 91 d, 40.8% after 126 d (end) 14C-phenyl Clodinafop-propargyl (2nd system): 47.4% after 91 d, 46.9% after 126 d (end) **Aerobic** study, 1 system, 9°C: 14C-pyridinyl Clodinafop-propargyl: 16.3% after 91 d, 52.2% after 357 d (end) **Anaerobic** study, 1 system, 20°C: 14C-pyridinyl Clodinafop-propargyl: 2.8% after 91 d, 7.0% after 245 d (end)
Distribution in water / sediment systems (active substance) ‡	**Aerobic** study (2 systems), 20°C: Rapid dissipation of Clodinafop-propargyl from water (not detectable from day 1 onwards), mainly due to degradation. Residues of Clodinafop-propargyl in sediment =0.6% AR from day 1 onwards. **Aerobic** (1 system), 9°C: Clodinafop-propargyl not detectable in water and sediment at first sampling (day 7). **Anaerobic** (1 system), 20°C: Clodinafop-propargyl not detectable in water and sediment at first sampling (day 28).
Distribution in water / sediment systems (metabolites) ‡	Metabolites >10% AR: **Aerobic** study (2 systems), 20°C: Water: **Clodinafop** (CGA 193469), max. 78.7-92.7% AR (d 1-2), not detectable from day 58 or 91 onwards **CGA 302371**, max. 16.6-32.3% AR (d 58-119), 11.5-15.6% AR on day 126-259 (end) Sediment: **Clodinafop** (CGA 193469), max. 28.0-29.6% AR (d 0-30), not detectable –1.8% AR on day 126-259 (end) **CGA 302371**, max. 8.1-13.5% AR (d 58-119), 7.5-7.6% AR on day 126-259 (end) **CGA 193468**, max. 8.0-10.0% AR (d 58-126), 7.1-8.0% AR on day 126 (end)

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

	Aerobic (1 system), 9°C: Water: **Clodinafop** (CGA 193469), max. 78.7% AR (d 14), not detectable from d 182 onwards **CGA 302371**, max. 18.9% AR (d 182), 12.2% AR (d 357 = end) Sediment: **CGA 193469**, max. 21.9% AR (d 63), 2.5% AR (d 357 = end) **Anaerobic** (1 system), 20°C: Water: **Clodinafop** (CGA 193469), max. 84.9% AR (d 91), 64.5% AR after 245 d = end Sediment: **CGA 193469**, max. 18.1% AR (d 28), 11.7% AR (d 245 = end)

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

Parent

Method of calculation	static water layer 30 cm deep **Clodinafop-propargyl** worst case DT_{50} (water) = 0.2 d **Clodinafop** (CGA 193469) highest percentage of formation in water (92.7%); correction for molar mass ratio = 311.7/349.8; worst case DT_{50} (water) = 68 d CGA 302371 highest percentage of formation in water (32.3%); correction for molar mass ratio = 147.4/349.8; TWA PECsw values equal to initial PECsw values. CGA 193468 highest percentage of formation in water (1.7%); correction for molar mass ratio = 239.6/349.8; TWA PECsw values equal to initial PECsw values.
Application rate	60 g a.s./ha
Main routes of entry	spray-drift emission (values taken from Guidance Document on Aquatic Ecotoxicology (8075/VI/97 rev 8 of 27.06.2001))

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

PEC$_{sw}$ (µg/L)																
day after app.	cereals, spring application, 60 g a.s./ha; PECsw of **Clodinafop-propargyl** at distance (drift %):															
	1 m (2.77%)		5 m (0.57%)		10 m (0.29%)		15 m (0.20%)		20 m (0.15%)		30 m (0.10%)		40 m (0.07%)		50 m (0.06%)	
	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC
0	0.55	0.55	0.11	0.11	0.058	0.058	0.040	0.040	0.030	0.030	0.020	0.020	0.014	0.014	0.012	0.012
1	0.017	0.15	0.004	0.032	0.002	0.016	0.001	0.011	0.001	0.008	0.001	0.006	4E-04	0.004	4E-04	0.003
2	0.001	0.080	1E-04	0.016	6E-05	0.008	4E-05	0.006	3E-05	0.004	2E-05	0.003	1E-05	0.002	1E-05	0.002
4	5E-07	0.040	1E-07	0.008	6E-08	0.004	4E-08	0.003	3E-08	0.002	2E-08	0.001	1E-08	0.001	1E-08	0.001
7	2E-11	0.023	3E-12	0.005	2E-12	0.002	1E-12	0.002	9E-13	0.001	6E-13	0.001	4E-13	0.001	3E-13	5E-04
14	5E-22	0.011	1E-22	0.002	5E-23	0.001	3E-23	0.001	3E-23	0.001	2E-23	0.000	1E-23	0.000	1E-23	2E-04
21	1E-32	0.008	3E-33	0.002	1E-33	0.001	1E-33	0.001	7E-34	4E-04	5E-34	3E-04	3E-34	2E-04	3E-34	2E-04
28	4E-43	0.006	8E-44	0.001	4E-44	0.001	3E-44	4E-04	2E-44	3E-04	1E-44	2E-04	1E-44	1E-04	9E-45	1E-04
35	1E-53	0.005	2E-54	0.001	1E-54	5E-04	8E-55	3E-04	6E-55	2E-04	4E-55	2E-04	3E-55	1E-04	3E-55	1E-04
42	3E-64	0.004	7E-65	0.001	4E-65	4E-04	2E-65	3E-04	2E-65	2E-04	1E-65	1E-04	9E-66	1E-04	7E-66	8E-05

day after app.	cereals, spring application, 60 g a.s./ha; PECsw of **Clodinafop** (CGA 193469) at distance (drift %):															
	1 m (2.77%)		5 m (0.57%)		10 m (0.29%)		15 m (0.20%)		20 m (0.15%)		30 m (0.10%)		40 m (0.07%)		50 m (0.06%)	
	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC	PEC	TWA PEC
0	0.46	0.46	0.094	0.094	0.048	0.048	0.033	0.033	0.025	0.025	0.017	0.017	0.012	0.012	0.010	0.010
1	0.45	0.46	0.093	0.094	0.047	0.048	0.033	0.033	0.025	0.025	0.016	0.016	0.011	0.012	0.010	0.010
2	0.45	0.45	0.092	0.093	0.047	0.047	0.032	0.033	0.024	0.025	0.016	0.016	0.011	0.011	0.010	0.010
4	0.44	0.45	0.090	0.092	0.046	0.047	0.032	0.032	0.024	0.024	0.016	0.016	0.011	0.011	0.010	0.010
7	0.43	0.44	0.088	0.091	0.045	0.046	0.031	0.032	0.023	0.024	0.015	0.016	0.011	0.011	0.009	0.010
14	0.40	0.43	0.082	0.088	0.042	0.045	0.029	0.031	0.021	0.023	0.014	0.015	0.010	0.011	0.009	0.009
21	0.37	0.41	0.076	0.085	0.039	0.043	0.027	0.030	0.020	0.022	0.013	0.015	0.009	0.010	0.008	0.009
28	0.34	0.40	0.071	0.082	0.036	0.042	0.025	0.029	0.019	0.022	0.012	0.014	0.009	0.010	0.007	0.009
35	0.32	0.38	0.066	0.079	0.034	0.040	0.023	0.028	0.017	0.021	0.012	0.014	0.008	0.010	0.007	0.008
42	0.30	0.37	0.061	0.077	0.031	0.039	0.022	0.027	0.016	0.020	0.011	0.013	0.008	0.009	0.006	0.008

cereals, spring application, 60 g a.s./ha; PEC (initial) = TWA PEC of CGA 302371 at:							
1 m (2.77%)	5 m (0.57%)	10 m (0.29%)	15 m (0.20%)	20 m (0.15%)	30 m (0.10%)	40 m (0.07%)	50 m (0.06%)
0.075	0.016	0.008	0.005	0.004	0.003	0.002	0.002

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

cereals, spring application, 60 g a.s./ha; PEC (initial) = TWA PEC of CGA 193468 at:							
1 m (2.77%)	5 m (0.57%)	10 m (0.29%)	15 m (0.20%)	20 m (0.15%)	30 m (0.10%)	40 m (0.07%)	50 m (0.06%)
0.006	0.001	0.001	5E-04	3E-04	2E-04	2E-04	1E-04

PEC_{SED} (mg/kg dw): not calculated as the endpoints of the toxicity tests with sediment-dwelling organisms were expressed in concentrations in the overlying water

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Modelling using **FOCUS-PEARL for Clodinafop-propargyl, Clodinafop** (CGA 193469) **and CGA 302371**, with appropriate FOCUSgw scenarios, according to FOCUS Guidance. Scenarios: winter cereals (Chateaudun, Hamburg, Jokioinen, Kremsmunster, Okehampton, Piacenza, Porto, Sevilla, Thiva); spring cereals (Chateaudun, Hamburg, Jokioinen, Kremsmunster, Okehampton, Porto). Average Kom, 1/n and DT50 values (corrected to pF 2) were used. The dose of the parent was corrected for interception by the crop (25%, with a resulting corrected dose of 0.045 kg as/ha) and the substance was applied directly to the ground at the corrected dose. The dose of metabolites was corrected for max. overall formation rate (%) and molar mass ratio (MMR) Clodinafop-propargyl: DT50 (20°C, pF 2) 0.7 d Kom 839 L/kg (1/n = 0.92) **Clodinafop** (CGA 193469) DT50 (20°C, pF 2) 12 d Kom 26.9 L/kg (1/n = 0.92) max. 100%, MMR = 311.7/349.8 CGA 302371 DT50 (20°C, pF 2) 10 d Kom 28.8 L/kg (1/n = 0.90) max. 40%, MMR = 147.4/349.8
Application rate	Single application. Uncorrected dose: 0.06 kg a.s./ha (cereals) Dose corrected for interception by the crop: 0.045 kg a.s./ha

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

	Time of application: 15 February - 1 May (winter wheat) 1 March – 15 May (spring wheat)
$PEC_{(gw)}$	
Maximum concentration	-
Average annual concentration (Results quoted for modelling with FOCUSgw scenarios, according to FOCUS guidance)	Average annual concentration (80th percentile) according to FOCUS guidance: Clodinafop-propargyl: <0.001 µg/L **Clodinafop** (CGA 193469): ≤0.001-0.002 µg/L **CGA 302371**: ≤0.001 µg/L (see detailed results in table below)

PEC(gw) - FOCUS modelling results

FOCUS scenario		80th percentile concentration in groundwater [µg/L] of:		
crop	location	Clodinafop-propargyl	CGA 193469	CGA 302371
winter cereals	Chateaudun	<0.001	<0.001	<0.001
	Hamburg	<0.001	0.001	<0.001
	Jokioinen	<0.001	<0.001	<0.001
	Kremsmunster	<0.001	0.001	<0.001
	Okehampton	<0.001	0.002	0.001
	Piacenza	<0.001	0.002	0.001
	Porto	<0.001	<0.001	<0.001
	Sevilla	<0.001	<0.001	<0.001
	Thiva	<0.001	<0.001	<0.001
spring cereals	Chateaudun	<0.001	<0.001	<0.001
	Hamburg	<0.001	0.001	<0.001
	Jokioinen	<0.001	<0.001	<0.001
	Kremsmunster	<0.001	0.001	<0.001
	Okehampton	<0.001	0.002	<0.001
	Porto	<0.001	<0.001	<0.001

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Modelling using **MACRO 4.0 for Clodinafop** (CGA 193469), for sand and clay site of UK field monitoring study (see above), treatment of winter wheat at 60 g CGA 193469/ha (corrected dose 40 g a.s./ha considering 30% crop interception and max. formation rate of 95.3%), application date 1 November on 29 successive years. **Clodinafop** (CGA 193469) DT50 (field) 29 d Koc 37 L/kg

PEC_{GW} (µg/L)

Maximum concentration	MACRO 4.0: peak concentration CGA 193469 in drainflow of clay soil: <0.01-3.00 µg/L (mean 1.01 µg/L)
Average annual concentration	MACRO 4.0: annual mean concentration CGA 193469 in percolate sand soil: <0.0001-0.0300 µg/L (mean 0.0035 µg/L)

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

Direct photolysis in air ‡	not available and not required
Quantum yield of direct phototransformation	not available and not required
Photochemical oxidative degradation in air ‡	(Atkinson method): Clodinafop-propargyl: DT_{50} 3.8-8.0 h **Clodinafop** (CGA 193469): DT_{50} 4.5-7.6 h **CGA 302371**: DT_{50} 16.2 h **CGA 193468**: DT_{50} 5.8 h
Volatilization ‡	from plant and soil surfaces: **Clodinafop-propargyl and Clodinafop** (CGA 193469): insignificant after 24 h

PEC (air)

Method of calculation	not calculated

$PEC_{(a)}$

Maximum concentration	not calculated

‡ 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 Definitions for risk assessment: clodinafop-propargyl, S-isomer of clodinafop propargyl[16], clodinafop (CGA 193469), S isomer of clodinafop[17] and CGA 302371 Definitions for monitoring: clodinafop-propargyl, S-isomer of clodinafop propargyl[4], clodinafop (CGA 193469) and S isomer of clodinafop[5] Water Ground water Definitions for risk assessment: clodinafop-propargyl, S-isomer of clodinafop-propargyl[4], clodinafop (CGA 193469), S isomer of clodinafop[5] and CGA 302371 Definitions for monitoring: clodinafop-propargyl, S-isomer of clodinafop-propargyl[4], clodinafop (CGA 193469) and S isomer of clodinafop[5] Surface water Definitions for risk assessment: clodinafop-propargyl (DT_{90} < 3 d), S-isomer of clodinafop-propargyl[4], clodinafop (CGA 193469), S isomer of clodinafop[5] and CGA 302371 Definitions for monitoring: clodinafop (CGA 193469), S isomer of clodinafop[5] Air Definitions for risk assessment: clodinafop-propargyl, S-isomer of clodinafop-propargyl[4], clodinafop (CGA 193469) and S isomer of clodinafop[5] Definitions for monitoring: clodinafop-propargyl, S-isomer of clodinafop-propargyl[4], clodinafop (CGA 193469) and S isomer of clodinafop[5]

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

Soil (indicate location and type of study)	not available
Surface water (indicate location and type of study)	not available

[16] prop-2-ynyl (*S*)-2-[4-(5-chloro-3-fluoro-pyridin-2-yloxy)-phenoxy]-propionionate
[17] (*S*)-2-[4-(5-chloro-3-fluoro-pyridin-2-yloxy)-phenoxy]-propionionic acid

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

Ground water (indicate location and type of study)	not available
Air (indicate location and type of study)	not available

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	none proposed

‡ 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} 2420 mg TOPIK 100EC/ kg bw (= 234 mg a.s./kg bw) LD_{50} 1392 mg a.s./kg bw
Reproductive toxicity to mammals ‡	Overall NOEC: 10 mg a.s./kg feed (0.32 mg a.s./kg bw/d) Ecotoxicologically relevant NOEC: 50 mg a.s./kg feed (4.6 mg a.s. /kg bw/d)
Acute toxicity to birds ‡	LD50 >1874 mg a.s./kg bw (mallard duck) LD50 1363 mg a.s./kg bw (bobwhite quail)
Dietary toxicity to birds ‡	LC50 >4872 mg a.s./kg feed (>1002 mg a.s./kg bw/d) (mallard duck) LC50 >4872 mg a.s./kg feed (>980 mg a.s./kg bw/d) (bobwhite quail)
Reproductive toxicity to birds ‡	NOEC 471 mg a.s./kg feed (82 mg a.s./kg bw/d) (mallard duck) NOEC 471 mg a.s./kg feed (43 mg a.s./kg bw/d) (bobwhite quail)

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

Toxicity/exposure ratios for **birds** (Annex IIIA, points 10.1)

Bird of 3000 g bw, DFI 1322 g/d, DWI 120 mL/d (early cereals, drinking water)
Bird of 100 g bw, DFI 113 g/d (earthworms)
Bird of 1000 g bw, DFI 206 g/d (fish)

Assessment in agreement with Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC (Draft Working Document Sanco/4145/2000, 25 Sept. 2002).

appln.	Time scale	Toxicity endpoint (mg a.s./kg bw/day)	Route	ETE (mg/kg bw/d)	TER	Annex VI trigger
cereals	acute	LD50: 1363(A)	cereals	3.7	368	10
cereals	acute	LD50: 1363(A)	small insects	3.2	426	10
cereals	acute	LD50: 1363(A)	Water	2.4E-05	6E+07	10
cereals	short-term	LC50: >980	Cereals	2.0	> 490	10
cereals	short-term	LC50: >980	small insects	1.8	> 544	10
cereals	long-term	NOEC: 43	Cereals	1.1	39	5
cereals	long-term	NOEC: 43	small insects	1.8	24	
cereals	long-term	NOEC: 43	earthworms	0.01	3325	5
cereals	long-term	NOEC: 43	Fish	5E-05	8E+05	5

(A) mg a.s./kg bw

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

Toxicity/exposure ratios for **mammals** (Annex IIIA, points 10.3) Mammal of 25 g bw, DFI 34.8 g/d, DWI 3.6 mL/d (cereals, drinking water) Mammal of 10 g bw, DFI 14 g/d (earthworms) Mammal of 3000 g bw, DFI 390 g/d (fish) Assessment in agreement with Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC (Draft Working Document Sanco/4145/2000, 25 September 2002).						
appln.	Time scale	Toxicity endpoint (mg a.s./kg bw/day)	route	ETE (mg/kg bw/d)	TER	Annex VI trigger
cereals	acute	LD50: 234 [1]	cereals	12	20	10
cereals	acute	LD50: 234 [1]	water	0.0001	300000	10
cereals	long-term	NOEC: 4.6	cereals	3.4	1.4[2]	5
cereals	long-term	NOEC: 4.6	earthworms	0.01	365	5
	long-term	NOEC: 4.6	fish	0.00003	20000	5

[1] mg a.s./kg bw
[2] Based on default DT50 = 10 days for degradation on food; implementation of a refined f_{twa} of 0.069 based on a realistic DT50 value of < 1 day in the risk assessment would result in TERlt of 10.

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)
Laboratory tests ‡				
Fish *Lepomis macrochirus*	Clodinafop-propargyl	96 h	LC_{50}	0.21
Fish *Lepomis macrochirus*	CGA 193469	96 h	LC_{50}	>76
Fish *Oncorhynchus mykiss*	CGA 193468	96 h	LC_{50}	5.7
Fish *Oncorhynchus mykiss*	CGA 302371	96 h	LC_{50}	>100
Fish *Oncorhynchus mykiss*	Topik 100 EC	96 h	LC_{50}	1.0
Fish *Oncorhynchus mykiss*	Clodinafop-propargyl	21 d	NOEC	0.10
Invertebrates *Crassostrea virginica*	Clodinafop-propargyl	96 h	EC_{50}	0.77
Invertebrates *Daphnia magna*	CGA 193469	48 h	EC_{50}	>10

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Invertebrates *Daphnia magna*	CGA 193468	48 h	EC_{50}	12
Invertebrates *Daphnia magna*	CGA 302371	48 h	EC_{50}	>100
Invertebrates *Daphnia magna*	Topik 100 EC	48 h	EC_{50}	0.37
Invertebrates *Daphnia magna*	Clodinafop-propargyl	21 d	NOEC	0.23
Invertebrates *Daphnia magna*	CGA 193469	22 d	NOEC	0.16
Algae *Scenedesmus subspicatus*	Clodinafop-propargyl	72 h	EbC_{50} / ErC_{50}	>1.6
Algae *Microcystis aeruginosa*	CGA 193469	120 h	EbC_{50} / ErC_{50}	42 / 71
Algae *Scenedesmus subspicatus*	CGA 193468	72 h	EbC_{50} / ErC_{50}	2.0 / 2.4
Algae *Selenastrum capricornutum*	CGA 302371	72 h	EbC_{50} / ErC_{50}	44 / >100
Algae *Selenastrum capricornutum*	Topik 100 EC	72 h	EbC_{50} / ErC_{50}	0.45 / >0.85
Aquatic plants *Lemna gibba*	Clodinafop-propargyl	14 d	EC_{50}	>1.4
Aquatic plants *Lemna gibba*	CGA 193469	14 d	EC_{50}	>4.5
Aquatic plants *Glyceria maxima*	Topik 240 EC	14 d	EC_{50}	0.15
Sediment-dwelling invertebrates				
NOEC = 1.2 mg a.s./L				

Microcosm or mesocosm tests
Not provided

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

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
cereals	0.06 (1X)	*Daphnia magna*	acute	1	379 (A)	100
		Lepomis macrochirus	acute	1	668	100
		Glyceria maxima	acute	1	271(A)	10
cereals	0.06 (1X)	*Oncorhynchus mykiss*	long-term	1	181	10
		Daphnia magna	long-term	1	415	10

(A) based on test with formulation

Bioconcentration

Bioconcentration factor (BCF) ‡	Clodinafop-propargyl 34 L/kg wwt (normalised to 6% lipid content)
Annex VI Trigger:for the bioconcentration factor	100 for not readily biodegradable compounds
Clearance time (CT_{50}) (CT_{90})	CT50: Clodinafop-propargyl 0.66 d (exposure to 0.21 µg/L) 0.45 d (exposure to 2.1 µg/L)
Level of residues (%) in organisms after the 14 day depuration phase	≤5% after 14 d depuration

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

Acute oral toxicity ‡	LD50 17.8 µg as/bee (Topik 100 EC) LD50 >93.7 µg as/bee (active substance)
Acute contact toxicity ‡	LD50 40.9 µg as/bee (Topik 100 EC)
Acute oral toxicity bumblebees	not available
Acute contact toxicity bumblebees	not available

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
cereals	0.06	Oral	3.4	50
		Contact	1.5	50

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

Field or semi-field tests
Not provided

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

Species	Test type and exposure duration	Test Substance	Dose (g as/ha)	Endpoint	Effect (%)	Annex VI Trigger (% / HQ)
Laboratory tests						
Predatory mites						
Typhlodromus pyri	laboratory, glass plate, 14 d	Topik 100 EC	4.0 7.9 16 32 63 127	survival / reproduction / overall LR50 HQ	13 / 11 / 7 30 / 11 / 24 48 / 8 / 61 72 / 6 / 83 77 / n.a. /- 82 / n.a. / - 20 g a.s./ha 2.9	2 (HQ)
Typhlodromus pyri	extended laboratory[(A)], 14 d	Topik 100 EC	5 10 30 60 90	survival / reproduction / overall LR50	12 / 9 / 5 25 / 9 / 19 32 / 8 / 34 30 / 9 / 23 43 / 7 / 51 >90 g a.s./ha	50%
Typhlodromus pyri	extended laboratory[(c)], 14 d	Topik 100 EC	5 60	survival / reproduction / overall LR50	17 / 9 / 15 35 / 8 / 38 >60 g a.s./ha	50%
Foliage dwelling predators						
Chrysoperla carnea	laboratory, glass plate	Topik 100 EC	2.4 60	survival / reproduction / overall	4 / 35 / 9 2 / 36 / 5	30%

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

Species	Test type and exposure duration	Test Substance	Dose (g as/ha)	Endpoint	Effect (%)	Annex VI Trigger (% / HQ)
Parasitoids						
Aphidius rhopalosiphi	laboratory, glass plate, 14 d	Topik 100 EC	0.031 0.12 0.50 2.0 7.9	survival / mummies/female / overall LR50	3 / 20 / 27 3 / 24 / 11 8 / 23 / 19 18 / 14 / 55 100 / n.a. / - 3.1 g a.s./ha	2 (HQ)
Aphidius rhopalosiphi	extended laboratory (A), 13 d	Topik 100 EC	27 40 60 90 135	Survival / mummies/female / overall LR50	3 / 20 / -4 3 / 18 / 2 3 / 17 / 9 0 / 17 / 5 3 / 18 / 6 >135 g a.s./ha	50%
Ground dwelling predators						
Poecilus cupreus	lab, direct spray of beetles and food on sand, 14 days	Topik 100 EC	2.4 60	Survival / food consumption LR50	0 / -1 0 / -1 >60 g a.s./ha	30%
Aleochara bilineata	extended lab, sprayed sand, 28 days	Topik 100 EC	5 10 30 60 90	hatched/female / reproduction / ER50	74 / 4 71 / 8 71 / 8 72 / 7 67 / 13 >90 g a.s./ha	50%

(A) Exposure to dry residues on laboratory treated isolated dwarf French bean leaves with Actipron surfactant.
(B) n.a. = not applicable.
(C) Exposure to dry residues on laboratory treated isolated dwarf French bean leaves.

Field or semi-field tests
Not provided

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

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

Acute toxicity ‡	Clodinafop-propargyl LC_{50} 197 mg/kg(A) CGA 193469 LC_{50} >1000 mg/kg(A) CGA 193468 LC_{50} 401 mg/kg(A) CGA 302371 LC_{50} 408 mg/kg(A) Topik 100 EC LC_{50} 28.3 mg as/kg(A)
Reproductive toxicity ‡	not available

(A) LC50 not corrected for organic content of OECD 207 substrate.

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

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
0.06	cereals	acute	353	10

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

Nitrogen mineralization ‡	**Clodinafop-propargyl** At 0.11 and 1.1 mg/kg resp., maximum effect 28 and 39% after 14 d, effects ≤16% after 28 d. **CGA 302371** At 0.02 and 0.10 mg/kg resp., maximum effect 51 and 57% after 28 d.
Carbon mineralization ‡	**Clodinafop-propargyl** At 0.11 and 1.1 mg/kg: effects <25%. **CGA 302371** At 0.02 and 0.10 mg/kg: effects <25%.

Effects on other non-target organisms (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Collembola: No data submitted.

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

Plants				
Species	Test type	Test Substance	Endpoint	Toxicity (g a.s./ha)
Carrot	Emergence Vegetative vigor	Topik 100 EC	ER50 germination and biomass ER50 biomass	>60 >60
Lettuce	Emergence Vegetative vigor	Topik 100 EC	ER50 germination and biomass ER50 biomass	>60 >60
Oat	Emergence Vegetative vigor	Topik 100 EC	ER50 germination and biomass ER50 biomass	>60 15
Oilseed rape	Emergence Vegetative vigor	Topik 100 EC	ER50 germination and biomass ER50 biomass	>60 >60
Onion	Emergence Vegetative vigor	Topik 100 EC	ER50 germination and biomass ER50 biomass	>60 >60
Pea	Emergence Vegetative vigor	Topik 100 EC	ER50 germination and biomass ER50 biomass	>60 >60

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

Respiratory rate	Clodinafop-propargyl EC_{50} >94 mg/L

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N: Dangerous to the environment R50/R53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment S60: This material and its container must be disposed of as hazardous waste S61: Avoid release to the 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
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median

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