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

tralkoxydim.

Finalised: 26 March 2008

SUMMARY

Tralkoxydim is one of the 79 substances of the third stage Part A of the review programme covered by Commission Regulation (EC) No 1490/2002[1]. This Regulation requires the European Food Safety Authority (EFSA) to organise upon request of the EU-Commission a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

The United Kingdom being the designated rapporteur Member State submitted the DAR on tralkoxydim in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 6 September 2005. The peer review was initiated on 3 March 2006 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 on during a written procedure in May – June 2007. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in October 2007.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in February-March 2008 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses for Southern Member States as a herbicide as proposed by the notifier, which comprises spraying applications, to control grass weeds in wheat and barley, at a single application. Full details of the application rates and timings can be found in the attached end points.

The representative formulated product for the evaluation was “Grasp 25 SC”, an aqueous suspension concentrate (SC), registered under different trade names in Europe.

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

Adequate methods are available to monitor tralkoxydim residues in plants, foodstuff of plant origin, soil and air. The residue definition for monitoring for ground water was defined as tralkoxydim and metabolite R173642[2], however validated monitoring method for this metabolite is not available.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

Mammalian toxicology of tralkoxydim was assessed in a series of tests. Tralkoxydim is rapidly and almost completely absorbed. It is widely distributed and rapidly excreted. It has no potential for accumulation and is extensively metabolised. It is of moderate oral toxicity and of low toxicity via the dermal and inhalative route. It is a mild skin- and eye irritant and not a skin sensitizer. A classification as Xn; R22 "Harmful if swallowed" is proposed. In short term toxicity tests with mice, rats, dogs and hamsters, overall, the liver and the adrenal glands were the main targets of toxicity. Tralkoxydim is not genotoxic. Based on increased incidences of Leydig cell tumours in male rats and increases in ovarian tumours in the carcinogenicity study in female hamsters a classification as Xn; Carc. Cat. 3 R40 "Limited evidence of a carcinogenic effect" is proposed. Based on adverse effects on gonads observed in hamster, dog and rat in subchronic and chronic studies a classification as Xn; Repr. Cat. 3 R62 "Possible risk of impaired fertility" is proposed. Based on postimplantation loss and malformations observed in rats and abortions and reduced litters in rabbits, a classification as Xn; Repr. Cat. 3 R63 "Possible risk of harm to the unborn child" is proposed. Based on these classifications the tralkoxydim metabolite R173642 was considered relevant according to the EU guideline Sanco/221/2000-rev.10. The acceptable daily intake (ADI) and the acceptable operator exposure level (AOEL) have been set at 0.005 mg/kg bw/d based on the effects observed in the 90-day and the 1-year dog study applying a safety factor of 100. The acute reference dose (ARfD) of 0.01 mg/kg bw has been derived from a rat developmental study applying a safety factor of 100. The exposure estimates for operators handling "Grasp 25 SC" are 88% of the AOEL without personal protective equipment (PPE), 82% with gloves during mixing and loading and 68% with gloves during mixing and loading and during application when applying the German model. The corresponding values when applying the UK POEM are 362%, 340% and 80% respectively. On the basis of the model proposed by Hoernicke et al., 1998[3] predicted exposure for re-entry workers is 4.5% of the AOEL. According to Lloyd and Bell, 1983[4] indicated exposure of bystanders will be 4% of the AOEL.

Tralkoxydim is extensively metabolised in cereals. A complex metabolic pattern was found in forage and straw. The proposed residue definition in cereal grains for monitoring and risk assessment is restricted to the parent compound only as residues of the parent compound and structurally related

[2] 3-(2,4,6-trimethylphenyl)pentanedioic acid
[3]Hoernicke *et al*., 1998. Hinweise in der Gebrauchsanleitung zum Schutz von Personen bei Nachfolgearbeiten in mit Pflantzenschutzmitteln behandelten Kulturen. Nachrichtenbl. Deut. Pflanzenschutzd. 50 (10), p 267.
[4]Lloyd and Bell, 1983. Hydraulic nozzles: comparative spray drift study.

metabolites are extremely low, far below analytically quantifiable levels. Supervised residue trials confirmed that residues of tralkoxydim in grains and straw are below 0.01 mg/kg in field conditions.
No transfer of residues from feed items to animal commodities at significant levels is expected. Residue definitions and MRLs are not needed for animal commodities.
No restriction needs to be considered for rotational crops.
Acute and chronic exposure assessments were conducted and did not show any risk for consumers.

As indicated in the physical-chemical section tralkoxydim exist in equilibrium of two isomeric forms (E and Z) which are both considered active substance. Data provided in the fate and behaviour section does not gives separated measurements of these isomers and it is not possible to know neither the relative amount at the equilibrium nor the rate of equilibration in the different environmental compartments. Risk assessment is assumed to cover both isomers at the proportion naturally occurring in the media tested.
Route of degradation of tralkoxydim in soil under dark aerobic conditions at 20 °C was investigated in two studies with a total of five soils. Rate of degradation is soil under dark aerobic conditions was also investigated in four studies additional to the route studies. According the results of these experiments tralkoxydim is low persistent in soil (DT_{50} = 1.1 – 6.1 d). Two major metabolites were identified: R173642 (max. 17.2 % AR after 15 d); R223068 (max. 12.5 % AR after 15 d). Metabolite R163434 (max. 7.5 % AR after 7 d) was found at levels above 5 % AR at two consecutive time points in one of the soils investigated. Mineralization was relatively high (CO_2 max. 55.1 % AR after 90 d) and unextractable radioactivity amounted to a maximum of 44.5 % after 90 d. The rate of degradation of the two major metabolites was investigated under dark aerobic conditions at 10 °C in a study with three soils. Additionally the rate of degradation of all the metabolites that need further assessment was calculated by multicompartmental model kinetic fitting of the data obtained in the studies performed with the parent compound. When values are normalized to 20 °C these studies show that R173642 is moderate to high persistent ($DT_{50\ norm\ 20C}$ = 12.1 – 112.1 d), R223068 is low to moderate persistent ($DT_{50\ norm\ 20\ C}$ = 2.0 – 22.4 d) and R163434 is low to moderate persistent ($DT_{50\ norm\ 20\ C}$ = 2.4 – 40.9 d).
PEC soil were calculated by the RMS based on worst case half life (parent compound) and maximum fraction observed for metabolites corrected for molecular weight (only max peak PEC soil calculated for metabolites).
Batch adsorption / desorption studies are available for tralkoxydim and metabolites R173642, R223068 and R163434 on six soils. Adsorption of tralkoxydim in soil was observed to be strongly pH dependent. Tralkoxydim may be considered to be very high mobile in slightly acidic soils (pH 6.8 K_{foc} = 30 mL / g) and only medium mobile in acidic soils (pH 5.4 K_{foc} = 290 mL / g). No experimental data is available on the adsorption / desorption behaviour in alkaline soils and values were extrapolated by the RMS from the available data to be used in modelling portential ground water contamination.
Also for metabolites R173642 and R223068 was observed a strong pH correlation with the adsorption. Metabolites R173642 and R223068 may be considered very high mobile in alkaline soils (R173642: pH 7.4 K_{foc} = 3 mL / g; R223068: pH 8.5 K_{foc} = 2.1 mL / g; for both metabolites

adsorption was negligible and not measurable in alkaline soils with low organic matter content) and medium mobile in the acidic ones (R173642: pH 5.1 K_{foc} = 210 mL / g; R223068: pH 5.1 K_{foc} = 360 mL / g) . Metabolite R163434 may be considered low to medium mobile (K_{foc} = 299 – 846 mL / g) and do not shows pH dependence.

Tralkoxydim hydrolysis is strongly pH dependent (pH 5: DT_{50} = 9.0 d; pH 7: DT_{50} = 140 d; pH 9: stable). The only hydrolysis product identified was R163434 (max. 76.8 % AR after 28 d, end of the study at pH 5) and does not suffer further hydrolysis at pH 5 and 7.

The aqueous photolysis study shows that photolysis may contribute to the dissipation of tralkoxydim in water. Two metabolites were formed at levels of 22 % AR: R159368 and R158378. Tralkoxydim is considered not to be readily biodegradable.

Fate and degradation of tralkoxydim was investigated in two dark water sediment studies. The pH of the water phase of those systems represents a worst case with respect to the hydrolysis stability of the parent compound; however, it does not cover the potential formation of hydrolysis metabolite R163434 in surface water. Member States may require further data to consider the effect of acidic surface water bodies on the aquatic fate of tralkoxydim. In the available study, tralkoxydim partition to the sediment was slow. Degradation in the whole system occurred with half lives of 60.1 to 161.3 d. Three metabolites were identified both in the water and sediment phases, however only metabolite R158378 exceeded 10 % AR in the sediment phase.

$PEC_{SW/SED}$ were calculated for tralkoxydim up to FOCUS Step 3 for the relevant scenarios and for metabolites R158378 (sediment phase of water sediment study, photolysis metabolite), R173642 (soil metabolite) and R223068 (soil metabolite) up to FOCUS Step 2. Also PEC_{SW} were calculated for the photolysis metabolites R158378 and R159368 based on conversion of the peak concentration observed for the parent at the Step 2 calculation for the molecular weight and the maximum observed in the aqueous photolysis study. Since the peak parent concentration for some FOCUS SW Step 3 scenarios is higher than the Step 2 values, EFSA calculated after the experts meeting the corresponding PEC SW for these metabolites that would result from using these more worst case estimates.

The 80th percentile annual average concentration, calculated with GW PELMO (v.3.3.2) model and the relevant scenarios, was below 0.1 µg / L for tralkoxydim and metabolites R223068 and R163434. However, the trigger of 0.1 µg / L was exceeded by metabolite R173642 for one (winter and spring) of the nine scenarios (max ann. av. 80th percentile PEC_{GW} = 0.435 µg / L). The need to assess the relevance of this metabolite was identified during the peer review. This metabolite was considered toxicological relevant based on the proposed classification of tralkoxydim agreed by the meeting of experts on toxicology (see section 2).

A data gap has been identified for PEC GW calculated with another FOCUS GW model following the recommendations of EFSA Opinion on FOCUS ground water models.

Tralkoxydim is not considered to be prone for long range transport and contamination through the atmosphere.

The acute toxicity of tralkoxydim is low to birds and mammals. Following the principles of the EU guideline SANCO/4145/2000 the acute and short-term risk to birds and the acute risk to mammals

were assessed to be low for the intended use of tralkoxydim in cereals. At Tier I Annex VI triggers were breached in the long-term scenario for both herbivorous and insectivorous birds and mammals. Refined assessment for Yellow wagtail and corn bunting as focal species indicated a low long-term risk to birds. Use of a revised endpoint in the long-term risk assessment for mammals indicated a low risk to insectivorous mammals but a high risk to herbivorous mammals and further refinement is still required.

Tralkoxydim is toxic to aquatic organisms, *Lemna gibba* as the most sensitive species. The risk to aquatic living organisms is considered low for tralkoxydim. The risk to metabolites is also considered to be low except for the photolytic metabolite R159368 where a potential high risk is identified at FOCUSsw Step 3 for one scenario applying 1/10 of parent toxicity data as surrogate endpoint in the risk assessment. The risk to bees, non-target arthropods, earthworms and soil living organisms is considered to be low. Risk mitigation comparable to 5 m buffer zones are required to protect non-target plants outside the treated field. The risk to biological methods of sewage treatment is considered to be low.

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

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BACKGROUND

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Tralkoxydim is one of the 79 substances of the third stage, part A, covered by the Regulation (EC) No 1490/2002 designating the United Kingdom as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, the United Kingdom submitted the report of its initial evaluation of the dossier on tralkoxydim, hereafter referred to as the draft assessment report, to the EFSA on 6 September 2005. In accordance with Article 11(2) of the Regulation (EC) No 1490/2002 the draft assessment report was distributed for consultation on 3 March 2006 to the Member States and the main applicant 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 during a written procedure in May – June 2007 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings in October 2007. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in February-March 2008 leading to the conclusions as laid down in this report.

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

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

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

- the comments received;
- the resulting reporting table (rev. 1-1 of 25 June 2007)

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

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

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

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Tralkoxydim is the ISO common name for (*RS*)-2-[(*EZ*)-1-(ethoxyimino)propyl]-3-hydroxy-5-mesitylcyclohex-2-en-1-one. It should be noted however, that due to keto-enol tautomerism, the C5 carbon of the cyclohexanone ring is not asymmetric and not subject to optical isomerism.

Tralkoxydim belongs to the class of cyclohexene oxime herbicides. It acts by the inhibition of the Acetyl CoA Carboxylase (ACCase) enzyme system, resulting in the inhibition of cell division in target weeds.
Tralkoxydim is used for the control of grass weeds in wheat and barley.

The representative formulated product for the evaluation was "Grasp 25 SC", an aqueous suspension concentrate (SC), containing 250 g/l technical material, registered under different trade names in Europe.

The representative uses evaluated comprise post-emergence applications with tractor-mounted hydraulic sprayer to control pernicious grass weeds such as Wild-oats (*Avena spp.*), Blackgrass (*Alopecurus myosuroides*), Ryegrasses (*Lolium spp.*), *Setaria viridis*, *Phalaris spp.* and *Apera spica-venti* in cereal crops, including wheat and barley up to crop growth stage BBCH 32, at a single application at a maximum rate of 450 g as/ha, in Southern Member States.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of tralkoxydim technical material (TC) is 960 g/kg, however the notifier confirmed that only the technical concentrate (TK) is currently manufactured. No FAO specifications exist for tralkoxydim. Tralkoxydim TK, a water-wet paste, as manufactured, contains a minimum of 780g/kg and a maximum of 900 g/kg tralkoxydim.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of tralkoxydim or the respective formulation. However it should be noted that the physical and chemical properties reported should be interpreted with caution as the *E/Z* isomer ratio is dependent on the sample environment and the values relate only to the conditions of the specific tests and may vary with varying conditions.
The enol form of tralkoxydim *E* isomer predominates in the solid state. In chloroform and other non-polar solvents tralkoxydim exists as two tautomeric forms in rapid equilibrium: a planar enol form and an aminoenone form, with the latter predominating. The tautomers cannot be separated by chromatography. In methanol and other nominally polar solvents tralkoxydim equilibrates between the two tautomers and a Z-oxime isomer.

The main data regarding the identity of tralkoxydim and its physical and chemical properties are given in appendix 1.
Adequate analytical methods are available for the determination of tralkoxydim in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.

Adequate methods are available to monitor tralkoxydim residues in food/feed of plant origin (wheat straw, wheat grain, orange, tomato, oat forage, oilseed); with an LOQ of 0.01mg/kg with a single MS/MS transition used for quantification.
Adequate methods are available to monitor tralkoxydim residues in soil (LOQ: 0.005mg/kg), water (LOQ: 0.05µg/l) and air (LOQ: 0.14 µg/m^3). However the residue definition for monitoring for ground water was defined as tralkoxydim and metabolite R173642 and a data gap for a monitoring method of this metabolite was set.

Analytical methods for the determination of residue in food/feed of animal origin and in body fluids and tissues are not required.

In conclusion, adequate methods are available to monitor tralkoxydim given in the respective residue definitions, except ground water, where a method for monitoring metabolite R173642 is missing.

2. Mammalian toxicology

Tralkoxydim was discussed at the PRAPeR meeting of experts for mammalian toxicology (PRAPeR 34, Round 7) in October 2007.

2.1 ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

Tralkoxydim is rapidly and nearly completely absorbed in rats after oral ingestion. It is excreted rapidly, approximately 29-58% via urine within 24 hours and 64-78% biliary within 48 hours. It is widely distributed. Highest concentrations can be found in liver and kidney. There was no evidence of accumulation. It is extensively metabolized. Only trace amounts of the applied dose remain as parent compound in excreta. In rats, the main metabolism pathway is oxidation of one of the methyl groups on the phenyl ring forming tralkoxydim alcohol which is further oxidised via an intermediary aldehyde metabolite forming tralkoxydim acid, the major urinary and biliary metabolite.

2.2 ACUTE TOXICITY

Tralkoxydim is of moderate acute toxicity in rats by the oral (LD_{50} 934 mg/kg bw) and of low toxicity by the dermal (LD_{50} > 2000 mg/kg bw) and inhalational route (LC_{50} > 3.5 mg/L). Tralkoxydim is a mild skin- and eye irritant but no classification was proposed based on the effects observed. Tralkoxydim is not a skin sensitizer. Based on the results obtained after oral application, classification as **Xn; R22 "Harmful if swallowed"** is proposed.

2.3 SHORT TERM TOXICITY

Short term effects of tralkoxydim were studied in rats in a 90-day dietary and in a 21-day dermal study, in mice in two 28-day dietary studies, in dogs in a 90-day and a 1-year oral study and in hamsters in a 90-day dietary study. Overall, liver and adrenal glands were the main target organs in these investigations.

In the rat dietary study the NOAEL was set at 20.5 mg/kg bw/d based on reduced bodyweight gain and food consumption, anaemia, increased kidney- and liver weights and changes in clinical chemistry while in the dermal study with rats no effects were observed up to the highest dose (NOAEL > 1000 mg/kg bw/d).

In the first mouse test a NOAEL was set at approximately 2 mg/kg bw/d based on increased absolute liver weights and liver lesions, while in the second investigation a NOAEL could not be derived since changes in clinical chemistry, increased liver weights, liver lesions and porphyria occurred already at the lowest dose (25 ppm). Because of hepatic porphyria and liver damage at low dose levels, the mouse was judged to be an inappropriate species to use for a carcinogenicity study.

In the hamster study haematological changes and increase in liver porphyrins were observed already at the lowest dose level (30 mg/kg bw/d) and a NOAEL could not be set. At higher dose changes in clinical chemistry, liver- and kidney effects were observed.

In the 90-day dog study the NOAEL was set at 0.5 mg/kg bw/d based on increased liver weight and liver enzyme activities and effects on liver (vacuolation, fatty change) and adrenals (vacuolation). A NOAEL of 0.5 mg/kg bw/d was derived also in the 1-year study based on elevated alkaline

phosphatase and alanine transaminase acivities and reduced potassium levels, discolouration and deposits in the gall bladder, increased liver and adrenal weights, fatty change in the liver and vacuolisation in adrenals at a dose of 5 mg/kg bw/d.

2.4 GENOTOXICITY

In the original DAR a standard test battery consisting of three *in vitro*- and two *in vivo* studies had been presented. However, while the *in vitro Salmonella* reverse mutation assay, the *in vitro* gene mutation assay with mouse lymphoma cells and the *in vivo* UDS test with rat hepatocytes were negative, the *in vitro* chromosomal aberration test with human lymphocytes and the *in vivo* micronucleus test in mice yielded equivocal results. An additional *in vivo* micronucleus test was provided in an addendum to the DAR, giving clear-cut negative results. The PRAPeR experts concluded that tralkoxydim had no genotoxic potential.

2.5 LONG TERM TOXICITY

A 2-year dietary study has been carried out in the rat, a 79-weeks feeding study and an 80-weeks carcinogenicity study have been conducted with hamsters.

In the rat study, reductions in body weight gain, food consumption, red blood cell parameters and cholesterol and increased lymphocyte counts and liver toxicity (increased ALT, increased clear hepatocytes, dark colour, increased liver weight, and increased haemosiderin) and retinal atrophy were seen. In addition, in males also enlarged testes and increased incidences of Leydig cell hyperplasia, tubular atrophy and reduced spermatozoa in the epididymides have been observed. The NOAEL for non-neoplastic findings has been set at 2.3 mg/kg bw/d. The neoplastic findings consisted of a moderate increase in the overall tumour burden, occurrence of astrocytomas and a moderately increased incidence of Leydig cell tumours in males. Following the suggestions of the applicant provided in an addendum to the DAR, the PRAPeR experts concluded that the astrocytomas and the increased overall tumour burden were not relevant for human risk assessment and the NOAEL for neoplastic findings was based on the occurrence of Leydig cell tumours and was set at 23.1 mg/kg bw/d.

Hamsters were selected as the second species for chronic studies instead of mice based on the findings described under “2.3 Short term toxicity”.

In the 79-week hamster study, marginal effects on body weight gain and food consumption were seen. In addition, diarrhoea, urinary incontinence, abnormal respiratory noises, reduced lymphocyte count, increased testes- and liver weight and lipofuscin accumulation in the liver was observed. The NOAEL was set at 14.8 mg/kg bw/d. There was no evidence of tumours. Based on the low survival rates and the marginal effects seen at the top dose, a NOAEL for carcinogenicity was not determined.

In the 80- weeks hamster study reductions in body weight gain and increased liver, kidney- and testes weights were observed and the non-neoplastic NOAEL was set at 138.9 mg/kg bw/d. In females increased incidences of ovarian tumours were observed. In an addendum to the DAR the applicant argued that the ovarian tumours were not treatment-related and thus not relevant. However, the PRAPeR experts did not dismiss the ovarian tumours and set a neoplastic NOAEL of 27.8 mg/kg bw/d based on these findings.

Based on the occurrence of neoplasms in rats and hamsters a classification as **Xn; Carc. Cat. 3 R40 "Limited evidence of a carcinogenic effect"** is proposed.

2.6 REPRODUCTIVE TOXICITY

A rat multigeneration study, two rat developmental studies and one rabbit developmental study are presented in the DAR.

In the multigeneration study reductions in body weight gain and food consumption in adults were observed. Mean body weight gain of offspring was persistently lower in all three generations at the top dose level. There were no treatment-related effects on the reproductive parameters. The NOAEL for reproduction was set at 91 mg/kg bw/d and the parental and offspring NOAELs are 18.2 mg/kg bw/d based on effects body weight gain and total litter weights respectively.

Based on the adverse effects on gonads observed in hamster, dog and rat in subchronic and chronic studies a classification as **Xn; Repr. Cat. 3 R62 "Possible risk of impaired fertility"** was proposed.

In the first rat developmental study severe maternal toxicity was evident at the top dose as deaths, weight loss during dosing, reduced body weight gain and food intake and gastro-intestinal changes occurred. Developmental effects consisted of reductions in litter sizes, gravid uterus-, litter- and mean foetal weight, increased postimplantation loss and increases in the incidence of external/visceral defects (oedema, pale spleen and cleft palate). Skeletal defects (mainly misshapen/fused vertebrae) were seen at the top dose and a single incidence of misshapen sacral vertebrae at the mid dose. The maternal and the developmental NOAELs were set at 30- and 3 mg/kg bw/d respectively.

In the second rat study, severe maternal toxicity was evident at 200 mg/kg bw/d (deaths, reduced body weight gain and food intake, gastro-intestinal changes). A significant reduction in mean foetal-, litter and mean gravid uterus weight was observed, the number of late intra-uterine deaths was slightly elevated and the incidence of foetuses with major defects (external/visceral and skeletal) was increased. The NOAEL for maternal toxicity was set at 3 mg/kg bw/d and that for developmental toxicity at 1 mg/kg bw/d.

In the rabbit severe maternal toxicity, reduced body weight and food consumption during dosing, a high rate of abortions, reduced implantations, live foetuses, foetuses per litter and a statistically significant increase in late intra-uterine deaths were observed. Teratogenic activity could not be evaluated at the higher doses because of the high abortion rate. The maternal and the developmental NOAEL were set at 20 mg/kg bw/d. The PRAPeR experts agreed to propose a classification for Tralkoxydim as **Xn; Repr. Cat. 3 R63 "Possible risk of harm to the unborn child".**

2.7 NEUROTOXICITY

Tralkoxydim is not a chemical belonging to any known group of neurotoxicants. Therefore, no specific neurotoxicity studies were considered necessary.

2.8 FURTHER STUDIES

Mechanistic studies

In a 28-day study with hamsters it was demonstrated that tralkoxydim is systemically available after oral ingestion and that it induces porphyria, liver enzymes and testosterone hydroxylation. In a 90-day study in the same species increased liver enzymes could be seen also but induction of porphyria by tralkoxydim could not be corroborated. In a further investigation it was observed that tralkoxydim is a strong porphyrinogenic agent in mice but not in rats, and that the substance most likely acts by inhibition of ferrochelatase activity, ultimately leading to accumulation of porphyrin in murine liver.

Two further studies in mice showed that tralkoxydim causes porphyria in this species.

In two studies elucidating potential species specific differences, it could be demonstrated that mice are very sensitive in regard to induction of porphyria, which was attributed to the inhibitory effect of tralkoxydim on ferrochelatase specifically in mice, while this effect did not occur in rats. In hamsters and guinea pigs a slight accumulation of porphyrin was found.

While *in vitro* it could be shown that tralkoxydim inhibits ferrochelatase activity in mouse hepatocytes resulting in an accumulation of porphyrin no such effects could be observed rat or human hepatocyte cultures suggesting that tralkoxydim would not cause porphyria in exposed humans and that this effect is species specific and consequently not relevant for human risk assessment.

In a 14-day repeated dose study with marmosets no porphyrin accumulation was seen in the liver. In a human study with male volunteers it was demonstrated that about 56% of tralkoxydim is excreted in urine as tralkoxydim acid and that peak excretion rates of tralkoxydim acid were achieved until 4 to 36 hours after administration. This indicates that the toxikokinetics of tralkoxydim are essentially similar in humans and experimental animals.

Metabolites

In the original DAR no studies on metabolites have been presented. However, in an addendum to the DAR a toxicological evaluation the tralkoxydim metabolite R173642[5] was provided as this metabolite was predicted to exceed an annual average concentration of 0.1 µg/L in groundwater for one (winter and spring) of the nine scenarios ((peak predicted concentration was 0.435 µg/L). R 173642 was negative in a battery of *in vitro* genotoxicity tests (*Salmonella* reverse mutation assay, mouse lymphoma assay, cytogenetic assay with human lymphocytes). The LD_{50} obtained in an acute oral toxicity test with rats was higher than 2000 mg/kg bw. From a 90-day dietary study in rats a NOAEL of 26.8 mg/kg bw/d was derived that was based on renal microlithiasis occurring at the next higher doses. The PRAPeR experts concluded that based on the properties of the parent compound (classification for carcinogenicity and reprotoxic effects is proposed) a possible concern of the metabolite was not covered by the studies presented and that consequently the metabolite had to be considered as being relevant according to the current EU guideline Sanco/221/2000-rev.10.

[5] R173642: 3-(2,4,6-trimethylphenyl)pentanedioic acid.

2.9 MEDICAL DATA

Four incidences of irritation reactions observed in manufacturing personnel handling tralkoxydim, and two cases of mild respiratory problems after inhalation and two cases of transient local irritant reactions after dermal contact with the concentrated formulation "Grasp 25 SC" in pesticide users were reported by the notifier.

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

ADI

The ADI is set at 0.005 mg/kg bw/d based on the NOAELs obtained in the 90-day and 1-year dog studies applying a safety factor of 100.

AOEL

The AOEL is as the ADI set at 0.005 mg/kg bw/d based on the NOAELs obtained in the 90-day and 1-year dog studies applying a safety factor of 100.

ARfD

The ARfD is set at 0.01 mg/kg bw based on the NOAEL obtained in a rat developmental study applying a safety factor of 100.

2.11 DERMAL ABSORPTION

In the original DAR an *in vitro* dermal penetration study with human epidermis was presented (no *in vivo* study was reported) suggesting to use dermal absorption values of 0.1- and 4.4% for the concentrate and the spray dilution respectively for "Grasp 25 SC". However, the validity of this study was contested. In an addendum to the DAR a new dermal *in vitro* penetration study with human epidermis performed with "Grasp 40SC" (concluded to be relevant to with "Grasp 25SC") was presented giving absorption values of 0.1 and 1.5% respectively. The PRAPeR expert agreed to use these values for the exposure assessment.

2.12 EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Grasp is a suspension concentrate (SC) containing 250 g tralkoxydim/L for use as a post-emergence herbicide on wheat and barley applied with tractor mounted broadcast boom sprayers at a maximum application rate of 0.45 g/ha and a maximum spray volume of 400 L/ha.

EFSA note: The UK POEM estimates are based on the minimum spray volume of 300 L/ha.

Operator exposure

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

Use/Method	Model	Without PPE	With PPE 1	With PPE 2
Wheat, Barley/vehicle mounted broadcast sprayer	German BBA	88%	82%	68%
	UK POEM	362%	340%	80%

PPE (personal protective equipment) PPE 1: gloves during mixing/loading, PPE 2: gloves during mixing and loading and during application.

Worker exposure

The estimates of exposure to tralkoxydim during crop inspections/rogueing activities for workers re-entering cereal crops treated with applications of 'GRASP 25 SC' are based on the German re-entry model proposed by Hoernicke et al., 1998[6]. Predicted exposure for re-entry workers is 4.5% of the short term systemic AOEL.

Bystander exposure

Predicted exposure for an unprotected bystander from application of 'GRASP 25 SC', based on published simulated bystander exposure studies relating to the use of field crop sprayers Lloyd and Bell, 1983[7] indicated exposure will be 4% of the short term systemic AOEL.

3. Residues

Tralkoxydim was discussed at the PRAPeR experts meeting for residues (PRAPeR 35, Round 7) in October 2007.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of tralkoxydim has been investigated in wheat in conditions of application similar to the proposed representative use in cereals. A complex metabolic pattern was observed in forage and straw, consisting of more than 10 individual compounds. The parent compound was not found. The major metabolites identified were R400307[8], R237434[9] and R209490[10] all present at 10 to 15 % of the Total Radioactive Residues (TRR, 1-2 mg/kg). The metabolic pathway proceeds through

[6]Hoernicke *et al*., 1998. Hinweise in der Gebrauchsanleitung zum Schutz von Personen bei Nachfolgearbeiten in mit Pflantzenschutzmitteln behandelten Kulturen. Nachrichtenbl. Deut. Pflanzenschutzd. 50 (10), p 267.
[7]Lloyd and Bell, 1983. Hydraulic nozzles: comparative spray drift study.
[8] R400307: 3-hydroxy-2-(imino-1-propyl)-5-dimethyl-4-hydroxymethylphenyl)cyclohex-2-enone
[9] R237434: 2,6-dimethyl-4-(2-ethyl-4,5,6,7-tetrahydrobenzoxazol-4-one)benzyl alcohol
[10] R209490: 3,5-dimethyl-4-(2-[1-(ethoxyimino)propyl]-3-hydroxycyclohex-2-enone-S-yl)benzyl alcohol

oxidation of the terminal methyl group of the phenyl ring, oxidative cleavage of the cyclohexyl ring and transformation of the ethoxyiminopropyl function. In grains, the TRR were low (0.01 - 0.02 mg/kg) and essentially non extractable.

The expert meeting considered the fact that the E/Z isomer ratio of the active substance may vary depending on the environmental conditions, meaning that the toxicological reference value may not exactly apply to the isomer mixture present in plants. Nevertheless it was agreed that this does not impact the risk assessment as practical consumer exposure is extremely low.

The residue definition proposed for monitoring and risk assessment purposes is tralkoxydim (sum of isomers) based on the fact that metabolism studies suggest that no residues of the parent compound or its structurally related metabolites are expected at measurable level in cereal grains. This residue definition is restricted to cereals. For other commodities the inclusion of metabolites in the residue definition should be considered based on specific metabolism studies.

A sufficient number of supervised residue trials (4 in wheat and 4 in barley, allowing extrapolation to rye, triticale and oats) is available to confirm that tralkoxydim residues in grains are below the Limit of Quantification (LOQ) of 0.01 mg/kg at harvest when applied in Southern Europe following the proposed representative use. In accordance with the information gained from the metabolism studies, tralkoxydim residues in straw are also below the LOQ. Metabolites were not analysed. The reliability of these trials is supported by storage stability studies demonstrating that tralkoxydim residues are stable under deep freeze conditions (-18°C) for at least 18 and 9 months in grains and straw respectively.

Processing studies were not conducted as residues in raw grains are below the LOQ and a maximum of 2% of the ADI is exhausted using worst case assumptions.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

The uptake and nature of the residues in succeeding crops planted into soil treated with tralkoxydim has been studied in leafy, root, legume and cereal crops. TRR were very low for all pre-planting intervals (30, 105 and 300 d) and in most cases below 0.05 mg/kg. The metabolic pattern was similar to that observed in primary crops, consisting of a complex mixture of highly polar metabolites individually present at low level. The identified metabolites were the same as in primary crops. No parent was present. This is consistent with the rapid and extensive degradation of tralkoxydim in soil.

Therefore, under practical conditions no residues of trakoxydim or its metabolites are expected in succeeding and rotational crops. Field trials and MRLs for succeeding and rotational crops are not necessary.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Residues of tralkoxydim are not present in cereal grains and straw. The only exposure of livestock results from the presence of metabolites in forage and straw.

Two metabolism studies in lactating goats were conducted, one with tralkoxydim and the other with one of its major metabolites (R237434) both being fed to animals at daily doses of 10 mg/kg. Tralkoxydim is absorbed and degraded to a very limited extend. It is present as clearly dominant compound in all edible tissues. Clear lipophylic behaviour was observed although not expected from

the physico-chemical properties of the active substance. The transfer of its metabolite R237434 is very limited and results in TRR below 0.05 mg/kg in all edible tissues. It is expected that the other metabolites observed in forage and straw present a similar behaviour due to their polarity.
Given the results of these metabolism studies, no residues of tralkoxydim and its metabolites are expected to be present at measurable level in animal tissues. No feeding studies need to be carried out. A residue definition and MRLs are not necessary for animal products.

3.3. CONSUMER RISK ASSESSMENT

No risk for consumers resulting from the representative use of tralkoxydim in cereals has been identified.

Chronic exposure

The chronic dietary exposure assessment has been based on the Theoretical Maximum Daily Intake (TMDI) calculation model of WHO using the WHO typical European diet for adult consumers. Residues in cereals were considered to be present at the level of the LOQ proposed as MRL. Under these conditions the potential consumer exposure was found to be below 1% of the ADI. Additionally, a National Estimated Daily Intake (NEDI) was carried out using the consumption pattern in UK for 10 population subgroups including infants, toddlers, children and adults (taking into consideration high individual consumption levels at the 97.5th percentile of the distribution of consumptions in the respective populations). The exposure of all consumer populations in UK was below 2% of the ADI.

Acute exposure

The acute exposure to residues of trakoxydim in wheat and barley grains has been assessed according to the WHO model for conducting National Estimates of Short Term Intakes (NESTI) calculations. Large portion consumption data for 10 population subgroups (including infants, toddlers, children and adults) in UK were used. Residues in cereals were considered to be present at the level of the LOQ proposed as MRL, and given the type of these commodities no variability factor was applied. This resulted in calculated potential acute exposures below 1% of the ARfD for adult populations of consumers.

3.4. PROPOSED MRLS

Based on the results of supervised residue trials MRLs in wheat, rye, triticale, barley and oats are proposed to be set below the LOQ of 0.01 mg/kg.

4. Environmental fate and behaviour

Tralkoxydim was discussed in the meeting of experts on fate and behaviour in the environment PRAPeR 32 (October 2007) on basis of the DAR and addendum 1 of September 2007.

As indicated in the physical-chemical section tralkoxydim exist in equilibrium of two isomeric forms (E and Z) which are both considered active substance. The relative proportion at the equilibrium depends on the state of the substance or the media in which it is solved. Data provided in the fate and behaviour section does not gives separated measurements of these isomers and it is not possible to know neither the relative amount at the equilibrium nor the rate of equilibration in the different environmental compartments. Risk assessment is assumed to cover both isomers at the proportion naturally occurring in the media tested.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Route of degradation of tralkoxydim (^{14}C labelled either at the phenyl or ciclohexyl ring) in soil under dark aerobic conditions was investigated in two studies with a total of five soils (pH 5.7 – 7.9; OM 1.1 – 4.7 %; clay 10 – 23 %). Two pairs of soils are given the same name. These soils were actually taken from the same site with some years of difference and have slightly different properties. The meeting of experts agreed to consider these as different soils and not as replicates for the purpose of this assessment.

Two major metabolites were identified in these studies: **R173642** (max. 17.2 % AR after 15 d); **R223068**[11] (max. 12.5 % AR after 15 d). Metabolite **R163434**[12] (max. 7.5 % AR after 7 d) was found at levels above 5 % AR at two consecutive time points in one of the soils investigated. Mineralization was relatively high (CO_2 max. 55.1 % AR after 90 d) and unextractable radioactivity amounted to a maximum of 44.5 % after 90 d.

A data gap was identified by the RMS for route and rate of degradation in soil studies under anaerobic conditions. The data gap was confirmed by the experts meeting that agreed that the data gap was not essential to finalize the EU risk assessment for the representative uses.

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

Rate of degradation is soil under dark aerobic conditions at 20 °C was investigated in four studies additional to the route studies. A total of seven soils were investigated, some of them of very similar characteristic since were obtained from the same site at different times (with some years of interval). The meeting of experts agreed to consider these soils as different for the purpose of this assessment. According the results of these experiments tralkoxydim is low to moderate persistent ($DT_{50\ norm\ 20\ °C}$ = 1.1 – 14.1 d).

The rate of degradation of two major metabolites was investigated under dark aerobic conditions at 10 °C in a study with three soils (pH 6.7 – 8.3, OM 1.9 – 5.6 %; clay 8 – 23 %). Additionally the rate of degradation of all the metabolites that need further assessment was calculated by multicompartmental model kinetic fitting of the data obtained in the studies performed with the parent compound. When values are normalized to 20 °C these studies show that R173642 is moderate to

[11] R223068: 4-[2-(1-{ethoxyimino}propyl)-3-hydroxy-2-cyclohexene-1-one-5-yl]-3,5-dimethyl benzoic acid

[12] R163434: 2-ethyl-4,5,6,7-tetrahydro-4-oxo-6-(2,4,6-trimethylphenyl)benzoxazole

high persistent ($DT_{50\ norm\ 20\ °C}$ = 12.1 – 112.1 d), R223068 is low to moderate persistent ($DT_{50\ norm\ 20\ C}$ = 2.0 – 22.4 d) and R163434 is low to moderate persistent ($DT_{50\ norm\ 20\ C}$ = 2.4 – 40.9 d).
PEC soil were calculated by the RMS based on worst case half life (parent compound) and maximum fraction observed for metabolites corrected for molecular weight (only max peak PEC soil calculated for metabolites).

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

Batch adsorption / desorption studies are available for tralkoxydim on six soils (pH_{H2O} 5.4 – 6.8; OM 0.5- 5.4 %; clay 5 – 47 %) and with metabolites R173642 on six soils (pH_{H2O} = 5.1 – 8.5; OM 1.0 – 5.1 %; clay 4 - 36 %), R223068 on six soils (pH_{H2O} = 5.1 – 8.5; OM 1.0 – 5.1 %; clay 4 - 36 %) and R163434 on 6 soils (pH_{H2O} = 5.3 – 7.8; OM 0.3 – 2.9 %; clay 6 - 44 %). Adsorption of tralkoxydim in soil was observed to be strongly pH dependent. Tralkoxydim may be considered to be very high mobile in slightly acidic soils (pH 6.8 K_{foc} = 30 mL / g) and only medium mobile in acidic soils (pH 5.4 K_{foc} = 290 mL / g). No experimental data is available on the adsorption / desorption behaviour in alkaline soils.
Also for metabolites R173642 and R223068 was observed a strong pH correlation with the adsorption. Metabolites R173642 and R223068 may be considered very high mobile in alkaline soils (R173642: pH 7.4 K_{foc} = 3 mL / g; R223068: pH 8.5 K_{foc} = 2.1 mL / g; for both metabolites adsorbtion was negligible and not measurable in alkaline soils with low organic matter content) and medium mobile in the acidic ones (R173642: pH 5.1 K_{foc} = 210 mL / g; R223068: pH 5.1 K_{foc} = 360 mL / g) . Metabolite R163434 may be considered low to medium mobile (K_{foc} = 299 – 846 mL / g). No pH adsorption relationship was observed for this later metabolite.
An aged (3 d) column leaching study was performed with ^{14}C labelled (phenyl and ciclohexyl rings) tralkoxydim with two soils (pH_{H2O} = 5.7 – 6.6; OM 2.0 – 4.3 %; clay 9 - 20 %). Up to 4.7 – 6.7 % AR was found in the leachate. However, it was not possible to identify single individual components on it. Consistent with the findings of the batch adsorption / desorption experiments; radioactivity in the leachate was highest with the higher pH.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Hydrolysis of ^{14}C labelled (phenyl and ciclohexyl rings) tralkoxydim was investigated in aqueous buffered solutions at pH 5, pH 7 and pH 9 at 25 °C. Tralkoxydim hydrolysis is strongly pH dependent (pH 5: DT_{50} = 9.0 d; pH 7: DT_{50} = 140 d; pH 9: stable). The only hydrolysis product identified was R163434 (max. 76.8 % AR after 28 d, end of the study at pH 5) that do not suffers further hydrolysis at pH 5 and 7.
Aqueous photolysis of ^{14}C labelled (phenyl and ciclohexyl rings) tralkoxydim was investigated in one study at 25 °C in aqueous buffered solutions (pH 9) with filtered (> 290 nm) Xenon lamp light simulating summer sun light in Florida (US 25- 35 °N) for 30 d. The study shows that photolysis may contribute to the dissipation of tralkoxydim in water. Two metabolites were formed at levels of 22 %

AR: **R159368**[13] and **R158378**[14]. No data is available of readily biodegradation of tralkoxydim that is considered not to be readily biodegradable.

Fate and degradation of tralkoxydim (^{14}C labelled in the phenyl or the ciclohexyl rings) in dark water sediment systems investigated in one study in two systems (pH_{water} = 7.9 – 8.3; pH_{sed} = 6.6 – 8.0, OM 3.0 – 4.6 % AR, clay 5 – 20 %) at 20 °C. The pH of the water phase represents a worst case with respect to the hydrolysis stability of the parent compound; however, it does not cover the potential formation of hydrolysis metabolite R163434 in surface water. Since most of the surface water in EU shows pH in the neutral-alkaline range the study may be considered representative enough for the EU risk assessment; however, Member States may required further data to consider the effect of acidic surface water bodies on the aquatic fate of tralkoxydim (data gap not essential to finalize EU risk assessment). In the available study, tralkoxydim partition to the sediment was slow and limited to levels of about 10 % AR. Degradation in the whole system occurred with half lives of 60.1 to 161.3 d. Three metabolites were identified both in the water and sediment phases, however only metabolite R158378 exceeded 10 % AR in the sediment phase.

$PEC_{SW/SED}$ were calculated for tralkoxydim up to FOCUS Step 3 for the relevant scenarios and for metabolites R158378 (sediment phase of water sediment study, photolysis metabolite), R173642 (soil metabolite) and R223068 (soil metabolite) up to FOCUS Step 2. Also PEC_{SW} were calculated for the photolysis metabolites R158378 and R159368 based on conversion of the peak concentration observed for the parent at the Step 2 calculation for the molecular weight and the maximum observed in the aqueous photolysis study. Since the peak parent concentration for some FOCUS SW Step 3 scenarios is higher than the Step 2 values, EFSA calculated after the experts meeting the corresponding PEC SW for these metabolites that would result from using these more worst case estimates.

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

Potential contamination of ground water by tralkoxydim and its soil metabolites R173642, R223068 and R163434, when used according the proposed representative uses, was assessed in the DAR with FOCUS GW PELMO (v.3.3.2) model and the relevant scenarios. Median temperature and moisture normalized (20 °C, pF2) laboratory degradation DT_{50} of tralkoxydim and its soil metabolites based in the complete available data set was used by the RMS for this calculation. Kinetic formation fraction of metabolites was derived from the studies performed with the parent compound. The pH dependence of K_{foc} of tralkoxydim, R173642 and R223068 was considered by the RMS calculating a specific K_{foc} for each scenario linearly interpolating of extrapolating from available experimental data. The meeting of MSs experts discussed this approach and found it acceptable taking into account the narrow pH range tested in the adsorption / desorption studies. The applicant's proposal of using extreme values instead of extrapolated ones was not accepted by the meeting. Mean or median values of 1/n were used as appropriate. The 80th percentile annual average concentration was below 0.1 µg /

[13] R159368: 3-hydroxy-2-propionyl-5-(2,4,6-trimethylphenyl)cyclohex-2-enone
[14] R158378: 3-hydroxy-2-(1-iminopropyl)-5-(2,4,6-trimethylphenyl)cyclohex-2-enone

L for tralkoxydim and metabolites R223068 and R163434 for the nine FOCUS scenarios. However, the trigger of 0.1 µg / L was exceeded by metabolite R173642 for one (winter and spring) of the nine scenarios (max ann. av. 80th percentile PEC_{GW} = 0.435 µg / L). The need to assess the relevance of this metabolite was identified during the peer review. This metabolite was considered to be toxicologically relevant by the meeting of experts on toxicology (see section 2) based on the proposed classification agreed for tralkoxydim.

During the peer review a need for further information to be provided by the applicant for the results of PEC GW obtained with a different FOCUS model following the EFSA Opinion on FOCUS GW models was identified.[15] The applicant presented new calculations that were assessed by the RMS in addendum 1. However, the end points used by the applicant in these new calculations differ considerable from those recommended by the RMS and agreed by the meeting of MSs experts. Therefore, a data gap is identified for PEC GW calculated with another FOCUS GW model following the recommendations of EFSA Opinion.

4.3. FATE AND BEHAVIOUR IN AIR

Tralkoxydim is considered only very slightly volatile on basis of its physicochemical properties. Photochemical oxidation in the atmosphere by OH· radicals is deemed to be short according available theoretical calculations (0.07 d). Therefore, tralkoxydim is not considered to be prone for long range transport and contamination through the atmosphere.

5. Ecotoxicology

Tralkoxydim was discussed in the meeting of experts on ecotoxicology (PRAPeR 33) in October 2007.

5.1. RISK TO TERRESTRIAL VERTEBRATES

Tralkoxydim is of low acute toxicity to birds and no effects were observed at the highest dose tested in reproduction studies with two different species.

The representative evaluated use of tralkoxydim is as herbicide in wheat and barley in southern Europe. The risk to large herbivorous birds (early application) and insectivorous birds (late application) for the cereal scenario was assessed in accordance with the Guidance Document on Risk Assessment for Birds and Mammals under Council Directive 91/414/EEC (SANCO/4145/2000). TER values for acute and short-term were above the Annex VI triggers (TER range: 67 – 83) indicating a low risk. For the long-term, TER values of 1.7 and 1.1 were derived for large herbivorous birds and small insectivorous birds respectively.

[15] Opinion of the Scientific Panel on Plant Protection Products and their Residues on a request of EFSA related to FOCUS groundwater models. The EFSA Journal (2004) 93, 1-20.

The long-term risk assessment for herbivorous birds was refined by using measured residue decline data from four studies conducted in southern France on cereals. By using the geometrical mean DT_{50} of 1.2 days, a refined estimated exposure was calculated resulting in along-term TER of 11.5. To refine the assessment for insectivorous birds, two bird species, skylark (*Alauda arvensis*) and corn bunting (*Milaria calandra*), were chosen. Both species consume mixed diets and dietary data were from Green (1978)[16] and Collinge (1924)[17]. The skylark diet was considered to be 44% seeds, 30% leaves and 26% invertebrates and the corn bunting diet 68% wild fruit, seeds and cereals, 23% small insects, 4% miscellaneous plant material categorised as grasses and cereal shoots, 2% slugs and earthworms. Four % of miscellaneous animal matter was added to the insects. Residues on weed seeds were assumed to degrade at the same rate as on foliage. Degradation of residues on insects was assumed not to occur. Based on the refined estimated exposure long-term TER values of 7.2 and 9.8 were derived for skylarks and corn bunting respectively. The risk to birds drinking from contaminated drinking water is considered low.

Documentation for selection of species and refinement of PD for insectivorous birds was requested during the review process. Notifier did submit a new field study to determine focal species in cereal fields in S-Europe (S-Spain). The study is evaluated in addendum 1 (September 2007). The expert meeting (PRAPeR 33) accepted Yellow wagtail and corn bunting as focal species and as representative for S-Europe. For yellow wagtail, diet was divided into 17% small and 87% large insects based on previous EU risk assessments. Use of a default DT50 of 10 days for dissipation of tralkoxydim in insects was accepted by the expert meeting as a further refinement, given the strong evidence of rapid dissipation of tralkoxydim in a variety of environmental compartments. The foliar DT_{50} is 1.2 days, the DT_{50} for aerobic soil in the dark is 2.6 days and the DT_{50} from the soil photolysis study is 1.96 days. A TER of 7.5 indicated an low risk to yellow wagtail. For corn bunting the UK studies on diet by Collinge (1924) mentioned above were used in the refined risk assessment. The approach was accepted by the expert meeting (PRAPeR 33), as it likely that a bird in S-Europe filling the same ecological niche has a similar diet composition. Use of standard default DT50 of 10 days (SANCO/4145/2000) for seeds and vegetation give TER of 5.9, indicating a low risk to corn bunting. The calculations were accepted by the expert meeting (PRAPeR 33).

The acute TER values for small herbivorous and insectivorous mammals are 10.5 and 235, respectively. This is above the Annex VI trigger of 10 and the acute risk is therefore considered to be low. There is no indication that the formulated product is more toxic than the active substance.

The long-term risk to mammals was originally assessed in the DAR by comparing the reproductive NOEC of 91 mg a.s./kg bw/day, which was the highest dose tested in a rat multigeneration study with the estimated theoretical exposure using the default time weight average factor of 0.53 for herbivorous mammals. This resulted in a first tier TER of 3.6 for herbivorous mammals. For

[16] Green R E (1978) Factors affecting the diet of farmland Skylarks (*Alauda arvensis*). Journ Ann Ecol 47, (913-928).
[17] Collinge W E (1924) The food of some British birds: a study in economic ornithology. (Self-published, York).

insectivorous mammals the TER_{lt} was calculated to 62.8. The assessment for herbivorous mammals was refined taking the determined DT_{50} value of 3 days for residue decline into account. This resulted in a refined TER_{lt} of 9.4.

Severe developmental effects were however observed in teratogenic studies with the rat and the NOAEL/NOEL for these effects was set to 1 mg a.s./kg bw/day. Furthermore, hepatic porphyria was observed at low doses in mice. Mice seem to be very susceptible to tralkoxydim-induced porphyria since the same effects were not observed in rats and hamsters at low doses. It was concluded that the species specific effect was not relevant to the human risk assessment. The effect might nevertheless be relevant for wild mice. The NOAEL for the liver effects was set to 2 mg a.s./kg bw/day. No reproduction study with mice is available and thus it is not known if mice reproduction could be affected at lower doses than for the rat.

Since the time window for teratogenic effects could be narrow, the NOAEL of 1 mg a.s./kg bw /day should be compared with a worst case exposure value for one day. The resulting TER values for herbivorous and insectivorous mammals would then be 0.02 and 0.69, respectively. This is 250 and 8 times below the Annex VI trigger and hence a high risk was identified for wild mammals.

PRAPeR 33 discussed the various potentially relevant long term data on mammals. It concluded that the liver porphyria effect may not be ecologically relevant and house mouse appears specifically sensitive. Other endpoints were therefore considered. From the original rat 3-generation study, the parental and developmental (offspring) NOAEL of 18.2 mg/kg bw/d (200 ppm) based on reduced body weight and food consumption in parents and reduced body weight gain in pups was considered potentially ecotoxicologically relevant. From the rat developmental study, a maternal NOAEL of 30 mg/kg bw/d and a developmental NOAEL of 1 mg/kg bw/d were concluded by the meeting on mammalian toxicology (PRAPeR 34). At the developmental LOEL of 3 mg/kg bw/d it was discussed whether the skeletal effects like fused vertebrae were relevant to ecological risk assessment. It was proposed not, but at 30 mg/kg bw/d some MS considered the skeletal effect (though not large) to be clearly dose related and ecologically relevant. Overall, however, PRAPeR 33 concluded that the effects at 30 mg/kg bw are slight and would in themselves probably not be ecologically relevant, therefore this was also a possible NOAEL. In the rabbit developmental study the meeting on mammalian toxicology (PRAPeR 34) concluded the maternal and developmental NOAEL to be 20 mg/kg bw/d (bolus dosing). There was a high incidence of abortions and a reduction in implantations and live foetuses, an increase in inter-uterine deaths and some skeletal malformations at the LOEL (the abortions were probably associated with gastro-intestinal effects). Therefore 20 mg/kg bw/d could also be an appropriate NOAEL. It was agreed at PRAPeR 33 that RMS should define a long-term endpoint taking in to account outcome of the meeting on mammalian toxicology.

RMS concluded that the NOAEL from the rat 3-generation study (18.2 mg/kg bw/d, with more relevant dosing method) should be chosen, this is comparable to the rabbit NOAEL of 20 mg/kg bw/d (bolus dosing). It should be noted that whilst the two endpoints are comparable in terms of mg a.s. kg

bw/day, as regards use in risk assessment they are not. The rat endpoint can be compared to a time-weighted average exposure estimate, whereas the rabbit endpoint can not. This is due to the fact that the effects seen in the rat study are considered to be due to continual or repeated exposure, whereas the endpoint from the rabbit study could be due to short-term exposure and hence a time-weighted average approach was not considered relevant. It was noted that the rat sub-chronic 90-day dietary study also gave a comparable NOAEL of 20.5 mg/kg bw/day.

Using a NOAEL of 18.2 mg/kg bw/d from the rat 3-generation study, the resulting TER values for herbivorous and insectivorous mammals are 0.7 and 12.6, respectively. Whereas the long-term risk is low for insectivorous mammal, further refinements of exposure factors (e.g. PD, C) are required for herbivorous mammals.

A risk assessment of birds drinking from both puddles and surface water is presented in addendum 1 (September 2007). TER values indicated a low risk and were accepted at PRAPeR 33. A TER value[18] indicating low risk to mammals drinking from puddles has subsequently been calculated by EFSA.

The $logP_{ow}$ for tralkoxydim was determined to be 2.1 and the bioconcentration factor to be 32 for whole fish. Hence the potential for bioaccumulation and secondary poisoning is considered as low.

5.2. RISK TO AQUATIC ORGANISMS

Based on the available acute toxicity data, tralkoxydim is classified as toxic to aquatic organisms. The lowest value was obtained for *Lemna gibba*, with an EC_{50} of 1.0 mg/L based on increase in biomass. Formulation studies were conducted with a 25% SC formulation (fish) and 'YF7763B' (invertebrates) and 'A-12706' (aq. plants). These formulations were considered sufficiently similar to 'Grasp 25CS' Acute toxicity studies are also available with fish, aquatic invertebrates and plants for the two major soil metabolites R173642 and R223068. Acute studies with invertebrates and plants are available for one of the aquatic photolysis metabolites, R158378. Chronic toxicity studies are available with fish and aquatic invertebrates using tralkoxydim technical as test material. A study with *Chironomus riparius* is available with the metabolite R158378 that was detected in amounts > 10 % of applied test material in the water/sediment study. For the photolysis metabolite R159368 and the soil metabolite R163434 10 × higher toxicity compared to tralkoxydim was assumed, since no study was available. No study on sediment dwelling organisms is required for tralkoxydim since it is a herbicide and the acute toxicity to *Daphnia* was found to be >0.1 µg/L.

Toxicity to exposure ratios were calculated with PEC_{sw} and PEC_{sed} FROM FOCUS Steps 1, 2 and 3 taking spray drift, run-off and drainage into account. As PECsw is higher in all FOCUS Step 3 scenarios than at FOCUS Step 2, the max PECsw from D2 ditch is used in the risk assessment. The only TER value for parent tralkoxydim that did not meet the Annex VI trigger using Step 1 values

[18] A TER of 19.8 is calculated with the following input parameters: 10 g mammal, daily water consumption of 1.57 ml/day, PECdrinking water of 300 mg a.s./L (tank concentration/5) and an acute toxicity of 934 mg/kg bw.

was the acute TER for fish and Lemna. However, using PEC_{sw} from Step 3 the TER was above the trigger. The risks from exposure to most metabolites is considered to be low at FOCUS Step 1, apart from the risk to fish calculated for R159368 based on the assumption that it is 10 x more toxic than the parent compound (TER_a >21.8). Based on the maximum FOCUS Step 3 PECsw for this metabolite of 8.7 µg a.s./L for the D2 ditch, the TER for fish would be >70 (trigger 100), at the next highest PECsw for the D1 ditch the TER would be >98.4. All other drainflow and run-off scenarios would pass at Step 3, including the South European scenarios which are relevant for the representative uses. These TERs are based on the direct transformation of tralkoxydim into R159368 at peak levels in laboratory photolysis studies. The PEC values are also based on maximum drainflow levels entering drainage ditches in the autumn following applications to winter cereals, therefore this level of photolysis is very worst case even in southern Europe where these drainflow scenarios are less relevant. Given that the toxicity endpoints are also 'greater than' values based on 10 x the toxicity of the parent compound, this adds to the very worst case nature of this assessment. In reality the risk to fish from R159368 in all Step 3 scenarios may be considered to be low. However, for formal reasons low risk should also be identified for both the D1 and D2 ditch scenarios. The risk assessment for the soil metabolite R163434 was undertaken by EFSA after the expert meeting

The bioconcentration factor for tralkoxydim was determined to 32 in whole fish and the potential for bioconcentration is thus considered to be low.

Concern was raised during the review process with regard to potential endocrine disrupting properties of tralkoxydim and the possible need for a full fish life cycle since effects on reproductive tissue were observed in mammals. However, these effects occurred after prolonged exposure at high dose levels of tralkoxydim. The NOEC from the rat multi-generation study of 200 ppm (18.2 mg/kg bw/d) based on growth effects is clearly lower than the levels indicating effects on reproductive organs of rats (500 ppm). No specific endocrine disrupting mode of action was identified in the mammalian toxicology studies. EFSA agrees to the conclusion of the RMS that no FFLC (fish full life cycle) study is required.

It can be concluded that the risk to aquatic organisms from exposure to tralkoxydim is low.

5.3. RISK TO BEES

Contact toxicity to bees was tested with tralkoxydim technical. No study on oral toxicity is available with the technical material since it was not sufficiently soluble in the feeding solution. Additionally, oral and contact toxicity of the formulation 'A-12706' were tested at a single nominal dose of 100 µg a.s/bee. The oral and contact HQ quotients calculated with the proposed application rate of 0.45 kg a.s/ha are clearly below the trigger of 50 and hence the risk to bees is considered to be low.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Studies on the two standard terrestrial arthropods, *Aphidius rhopalosiphi* and *Typhlodromus pyri* were conducted with the formulation 'YF 7763B' which was confirmed by the applicant to be identical to

'Grasp 25CS'. Hazard quotients (HQ) for in-field were calculated based on the LR_{50} values obtained for these species in glass plate tests and found to be <1.0. No separate off-field assessment is considered necessary since the in-field HQ values are below the ESCORT II trigger.

Additional laboratory tests using the ground-dwelling species, *Poecilus cupreus* and *Pardosa* spp. with another tralkoxydim SC formulation showed no mortality or sublethal effects. Thus, it can be concluded that the risk to non-target arthropods from the evaluated use of tralkoxydim is low.

5.5. RISK TO EARTHWORMS

The acute toxicity of tralkoxydim and the major metabolites R173642 and R223068 to earthworms is low. Also the acute toxicity of the formulation 'A-12706' which was confirmed by the applicant to be identical to 'Grasp 25CS' is low. All acute TER values calculated based on initial PEC_{soil} are more than 2 orders of magnitude above the Annex VI trigger of 10 and the risk is therefore considered to be low

The DT_{90} in soil for tralkoxydim and the metabolites R173642 and R223068 is <90 days and only one application is foreseen, hence there is no requirement to consider long term risk.

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

Since the DT_{90}s in soil for tralkoxydim and the soil metabolites R173642, R223068 and R163434 are <100 days, additional studies on soil macro-organisms are not required according to the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002) and the risk is considered to be low.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The tralkoxydim formulation JF9517 and the soil metabolites R173642 and R223068 showed no effects >25% on soil respiration and nitrogen transformation at a dose rate four times higher than the estimated PEC_{soil} after 28 days when compared to the control. The RMS did not consider the formulation JF9517 (EC formulation) as comparable to Grasp® (SC formulation), but to be worst case, as EC formulations are generally more toxic than SC formulations. This was accepted by the expert meeting (PRAPeR 33).

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

Pre- and post-emergence effects on ten species of non-target plants (*Glycine max, Cucumis sativus, Lycopersicon esculentum, Lactuca sativa, Brassica oleracea, Brassica rapa, Zea mays, Allium cepa, Avena sativa, Lolium* perenne) were tested using a water-soluble pellet formulation of tralkoxydim. No effects were observed on dicotyledons at the maximum treatment level of 260 g a.s./ha. Post-emergence effects on growth were seen on monocotelydons. The most sensitive endpoint was shoot length, with an ER_{50} of 32 g a.s./ha obtained for *Zea mays*.

Based on 2.77% spray drift at 1 m distance from the field a TER of 2.6 was calculated. With risk mitigation measures comparable to 5 m buffer zones the spray deposition will be reduced to 2.57 g a.s./ha and the corresponding TER will be 12.5.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

Data from an available tests with technical tralkoxydim showed <10% inhibition of respiration rate of activated sludge micro-organisms up to 100 mg tralkoxydim/L. Should tralkoxydim reach sewage treatment plants the risk the risk for adverse effects is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: tralkoxydim, R173642, R223068 and R163434.
Definitions for monitoring: tralkoxydim

Water

Ground water

Definitions for exposure assessment: tralkoxydim, R173642, R223068 and R163434.
Definitions ground water.

Surface water

Definitions for risk assessment: tralkoxydim, R158378 (sediment and aqueous photolysis metabolite), R159368 (photolysis metabolite), R173642 (from soil), R223068 (from soil) and R163434 (from soil).
Definitions for monitoring: tralkoxydim

Air

Definitions for risk assessment: tralkoxydim
Definitions for monitoring: tralkoxydim

Food of plant origin

Definitions for risk assessment: tralkoxydim (sum of isomers)
Definitions for monitoring: tralkoxydim (sum of isomers)

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**
Tralkoxydim	low to moderate persistent ($DT_{50\ norm\ 20\ °C}$ = 1.1 – 14.1 d)	Low risk to birds and mammals, except for long-term risk to herbivorous mammal where further refinements are required to identify low risk. Risk mitigation is required for non-target plants off-field. Low risk to all other non-target organisms
R173642	moderate to high persistent ($DT_{50\ norm\ 20\ °C}$ = 12.1 – 112.1 d)	Low risk
R223068	low to moderate persistent ($DT_{50\ norm\ 20\ °C}$ = 2.0 – 22.4 d)	Low risk
R163434	low to moderate persistent ($DT_{50\ norm\ 20\ C}$ = 2.4 – 40.9 d)	No data available, no data required

* Half life values in this table are normalized for temperature to 20 °C but not for soil moisture content.

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**
Tralkoxydim	Very high mobile in slightly acidic soils (pH 6.8 K_{foc} = 30 mL / g); medium mobile in acidic soils (pH 5.4 K_{foc} = 290 mL / g). No experimental data available in alkaline soils.	FOCUS: No	Yes	Relevant.	Low risk (Lowest effect level is detected for *Lemna gibba*: EbC50 = 1 mg/L)

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
R173642	Very high mobile in alkaline soils (pH 7.4 K_{foc} = 3 mL / g); medium mobile in the acidic ones (pH 5.1 K_{foc} = 210 mL/ g)	FOCUS GW: Yes (trigger of 0.1 µg /L exceeded for two of nine scenarios with FOCUS PELMO v.3.3.2; data gap identified for calculations with a second FOCUS model).	No R173642 is 100 x less toxic than the parent to higher aquatic plants	Relevant based on proposed classification of the parent and consequent lack of data showing non- relevance.	Risk considered low. (Lowest effect level is detected for *Daphnia magna*: EC50 = 85 mg/L)
R223068	very high mobile in alkaline soils (pH 8.5 K_{foc} = 2.1 mL / g); medium mobile in the acidic soils (pH 5.1 K_{foc} = 360)	FOCUS GW: No	No assessed, no assessment required.	No assessed, no assessment required.	No data available. No data required
R163434	low to medium mobile (K_{foc} = 299 – 846 mL / g)	FOCUS GW: No	No assessed, no assessment required.	No assessed, no assessment required.	No data available. No data required

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
tralkoxydim (water and sediment)	Low risk
R158378 (sediment and aqueous photolysis metabolite)	Low risk
R159368 (aqueous photolysis metabolite)	Potentially high risk identified for one scenario at FOCUSsw Step 3 applying 1/10 of parent toxicity data as surrogate endpoint in the risk assessment.

Compound (name and/or code)	**Ecotoxicology**
R173642 (from soil)	Low risk
R223068 (from soil)	Low risk
R163434 (from soil)	Low risk

Air

Compound (name and/or code)	**Toxicology**
tralkoxydim	Not acutely toxic by inhalation (LC_{50} > 3.5mg/L)

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

- A data gap for a monitoring method for metabolite R173642 in ground water was identified (relevant for all representative uses evaluated; submission date unknown; refer to point 2.8)
- A data gap for carcinogenicity, reproductive and developmental toxicity for the metabolite R173642 was identified based on the classification of the parent compound.
- A data gap was identified for route and rate of degradation studies in soil studies under anaerobic conditions (not considered essential to finalize EU risk assessment of representative uses evaluated /; no submission date proposed by the notifier; refer to point 4.1).
- A data gap was identified to address degradation of tralkoxydim in water/sediment studies in acidic surface water bodies (not considered essential to finalize EU risk assessment of representative uses evaluated /; no submission date proposed by the notifier; refer to point 4.2).
- A data gap has been identified for PEC GW for tralkoxydim and soil metabolites calculated with another FOCUS GW model (PEARL) following the recommendations of EFSA Opinion on FOCUS ground water models and using the input parameters agreed during the peer review (relevant for all representative uses evaluated /; no submission date proposed by the notifier; refer to point 4.2.2).
- A data gap has been identified for a refined assessment for the long-term risk to herbivorous mammal. (relevant for all representative uses evaluated; submission date to be proposed by the notifier; refer to point 5.1)
- A data gap is identified to clarify the potential high risk of the photolysis metabolite R158378 to aquatic organisms in one FOCUSsw step 3 scenario, either by providing toxicity effect data for the metabolite or by refining the exposure estimate. (relevant for all representative uses evaluated; submission date to be proposed by the notifier; refer to point 5.2)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses for Sounthern Member States as proposed by the applicant which comprises post-emergence applications with tractor-mounted hydraulic sprayer to control pernicious grass weeds such as Wild-oats (*Avena spp*.), Blackgrass (*Alopecurus myosuroides*), Ryegrasses (*Lolium spp*.), *Setaria viridis*, *Phalaris spp*. and *Apera spica-venti* in cereal crops, including wheat and barley up to crop growth stage BBCH 32, at a single application at a maximum rate of 450 g as/ha.

The representative formulated product for the evaluation was “Grasp 25 SC”, an aqueous suspension concentrate (SC), containing 250 g/l tralkoxydim technical material, registered under different trade names in Europe.

Adequate analytical methods are available for the determination of tralkoxydim residues in food of plant origin, soil, water and air, however a data gap was set for a method for monitoring metabolite R173642 in ground water.
Sufficient analytical methods as well as methods relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection products are possible.

Tralkoxydim is absorbed rapidly and almost completely in the rat after oral uptake. It is widely distributed and rapidly excreted. It has no potential for accumulation. It is extensively metabolised. Only trace amounts remained as parent compound in the excreta. The main metabolism pathway is oxidation forming alcohol which is further oxidised via an intermediary aldehyde to the main metabolite tralkoxydim acid. It is of moderate oral toxicity and of low toxicity via the dermal and inhalative route. It is a mild skin- and eye irritant and not a skin sensitizer. A classification as **Xn; R22 "Harmful if swallowed"** is proposed.
In short term toxicity tests with mice, rats, dogs and hamsters, overall, the liver and the adrenal glands were the main targets of toxicity. The dog was the most sensitive species. Tralkoxydim does not have a genotoxic potential. A long term dietary study has been carried out in rats and a chronic and a carcinogenicity study have been conducted in hamsters since the mouse was considered to be an inadequate species because of the occurrence of porphyria already at low doses in short term tests. Based on increased incidences of Leydig cell tumours in male rats and increases in ovarian tumours in the carcinogenicity study in female hamsters a classification as **Xn; Carc. Cat. 3 R40 "Limited evidence of a carcinogenic effect"** is proposed. Based on adverse effects on gonads observed in hamster, dog and rat in subchronic and chronic studies a classification as **Xn; Repr. Cat. 3 R62 "Possible risk of impaired fertility"** is proposed. Since in developmental studies postimplantation loss and malformations have been observed in rats and abortions and reduced litters in rabbits, a classification as **Xn; Repr. Cat. 3 R63 "Possible risk of harm to the unborn child"** is proposed.
On the basis of the proposed classification for tralkoxydim, the metabolite R173642 is considered relevant according to the EU guideline Sanco/221/2000-rev.10.
The acceptable daily intake (ADI) and the acceptable operator exposure level (AOEL) have been set at 0.005 mg/kg bw/d based on the effects observed in the 90-day and the 1-year dog study applying a safety factor of 100. The acute reference (ARfD) dose of 0.01 mg/kg bw has been derived from a rat developmental study applying a safety factor of 100. The exposure estimates for operators handling "Grasp 25 SC" are 88 % without personal protective equipment (PPE), 82% with gloves during mixing and loading and 68% with gloves during mixing and loading and during application applying the German model. The corresponding values when applying the UK POEM are 362%, 340% and 80% respectively. On the basis of the model proposed by Hoernicke et al., 1998[19] predicted exposure for re-entry workers is 4.5% of the AOEL. According to Lloyd and Bell, 1983[20] indicated exposure of bystanders will be 4 % of the AOEL.

[19]Hoernicke *et al*., 1998. Hinweise in der Gebrauchsanleitung zum Schutz von Personen bei Nachfolgearbeiten in mit Pflantzenschutzmitteln behandelten Kulturen. Nachrichtenbl. Deut. Pflanzenschutzd. 50 (10), p 267.
[20]Lloyd and Bell, 1983. Hydraulic nozzles: comparative spray drift study.

Tralkoxydim is extensively metabolised in cereals. A complex metabolic pattern was found in forage and straw. The proposed residue definition in cereal grains for monitoring and risk assessment is restricted to the parent compound only as residues of the parent compound and structurally related metabolites are extremely low, far below analytically quantifiable levels. Supervised residue trials confirmed that residues of tralkoxydim in grains and straw are below 0.01 mg/kg in field conditions.
No transfer of residues from feed items to animal commodities at significant levels is expected. Residue definitions and MRLs are not needed for animal commodities.
No restriction needs to be considered for rotational crops.
Acute and chronic exposure assessments were conducted and did not show any risk for consumers.

As indicated in the physical-chemical section tralkoxydim exist in equilibrium of two isomeric forms (E and Z) which are both considered active substance. Data provided in the fate and behaviour section does not gives separated measurements of these isomers and it is not possible to know neither the relative amount at the equilibrium nor the rate of equilibration in the different environmental compartments. Risk assessment is assumed to cover both isomers at the proportion naturally occurring in the media tested.
According the results of the available aerobic route and rate degradation in soil studies tralkoxydim is low to moderate persistent in soil. Two major metabolites were identified: R173642; R223068. Metabolite R163434 was found at levels above 5 % AR at two consecutive time points in one of the soils investigated. Mineralization was relatively high (CO_2 max. 55.1 % AR after 90 d) and unextractable radioactivity amounted to a maximum of 44.5 % after 90 d. When values are normalized to 20 ^{o}C the available studies show that R173642 is moderate to high persistent in soil, R223068 is low to moderate persistent and R163434 is low to moderate persistent in soil.
PEC soil were calculated by the RMS based on worst case half life (parent compound) and maximum fraction observed for metabolites corrected for molecular weight (only max peak PEC soil calculated for metabolites).
Adsorption of tralkoxydim in soil was observed to be strongly pH dependent. Tralkoxydim may be considered to be very high mobile in slightly acidic soils and only medium mobile in acidic soils. No experimental data is available on the adsorption / desorption behaviour in alkaline soils and values were extrapolated by the RMS from the available data to be used in modelling potential ground water contamination.
Also for metabolites R173642 and R223068 was observed a strong adsorption correlation with the pH. Metabolites R173642 and R223068 may be considered very high mobile in alkaline soils and medium mobile in the acidic ones. Metabolite R163434 may be considered low to medium mobile and does not show pH dependence.
Tralkoxydim hydrolysis is strongly pH dependent (pH 5: DT_{50} = 9.0 d; pH 7: DT_{50} = 140 d; pH 9: stable). The only hydrolysis product identified was R163434 (max. 76.8 % AR after 28 d, end of the study at pH 5) and does not suffer further hydrolysis at pH 5 and 7.

The aqueous photolysis study shows that photolysis may contribute to the dissipation of tralkoxydim in water. Two metabolites were formed at levels of 22 % AR: R159368 and R158378. Tralkoxydim is considered not to be readily biodegradable.

Fate and degradation of tralkoxydim was investigated in two dark water sediment studies. Member States may required further data to consider the effect of acidic surface water bodies on the aquatic fate of tralkoxydim. In the available study, tralkoxydim partition to the sediment was slow. Degradation in the whole system occurred with half lives of 60.1 to 161.3 d. Three metabolites were identified both in the water and sediment phases, however only metabolite R158378 exceeded 10 % AR in the sediment phase.

$PEC_{SW/SED}$ were calculated for tralkoxydim up to FOCUS Step 3 for the relevant scenarios and for metabolites R158378 (sediment phase of water sediment study, photolysis metabolite), R173642 (soil metabolite) and R223068 (soil metabolite) up to FOCUS Step 2. Also PEC_{SW} were calculated for the photolysis metabolites R158378 and R159368 based on conversion of the peak concentration observed for the parent at the Step 2 calculation for the molecular weight and the maximum observed in the aqueous photolysis study. Since the peak parent concentration for some FOCUS SW Step 3 scenarios is higher than the Step 2 values, EFSA calculated after the experts meeting the corresponding PEC SW for these metabolites that would result from using these more worst case estimates.

The trigger of 0.1 µg / L 80^{th} percentile annual average concentration was exceeded by metabolite R173642 for one (spring and winter) of the nine scenarios modelled with FOCUS GW PELMO model. On the basis of the proposed classification for tralkoxydim, this metabolite was concluded to be toxicological relevant by the meeting of experts on toxicology (see section 2).

A data gap has been identified for PEC GW calculated with another FOCUS GW model following the recommendations of EFSA Opinion on FOCUS ground water models.

Tralkoxydim is not considered to be prone for long range transport and contamination through the atmosphere.

The acute toxicity of tralkoxydim is low to birds and mammals. Following the principles of the EU guideline SANCO/4145/2000 the acute and short-term risk to birds and the acute risk to mammals were assessed to be low for the intended use of tralkoxydim in cereals. At Tier I Annex VI triggers were breached in the long-term scenario for both herbivorous and insectivorous birds and mammals. Refined assessment for Yellow wagtail and corn bunting as focal species indicated a low long-term risk to birds. Use of a revised endpoint in the long-term risk assessment for mammals indicated a low risk to insectivorous mammals but a high risk to herbivorous mammals and further refinement is still required.

Tralkoxydim is toxic to aquatic organisms, *Lemna gibba* as the most sensitive species. The risk to aquatic living organisms is considered low for tralkoxydim. The risk to metabolites is also considered to be low except for the photolytic metabolite R159368 where a potential high risk is identified at FOCUSsw Step 3 for one scenario applying 1/10 of parent toxicity data as surrogate endpoint in the risk assessment. The risk to bees, non-target arthropods, earthworms and soil living organisms is considered to be low. Risk mitigation comparable to 5 m buffer zones are required to protect non-

target plants outside the treated field. The risk to biological methods of sewage treatment is considered to be low.

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

- Low risk has not been identified for the photolytic metabolite R159368 in the aquatic risk assessment for one of the FOCUSsw step 3 scenarios.
- For the intended use risk mitigation e.g. non-spray buffer zones of 5 m is required to identify a low risk to non-target plants

Critical areas of concern

- Metabolite R173642 may exceed 0.1 µg / L 80th percentile annual average ground water concentration under vulnerable conditions.
- Metabolite R173642: Data on carcinogenicity, reproductive and developmental effects that would demonstrate that this metabolite is not relevant according to the EU guideline SANCO/221/2000-rev.10 have not been provided.
- The long-term risk to herbivorous mammals needs to be addressed.

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) ‡	Tralkoxydim
Function (*e.g.* fungicide)	Herbicide

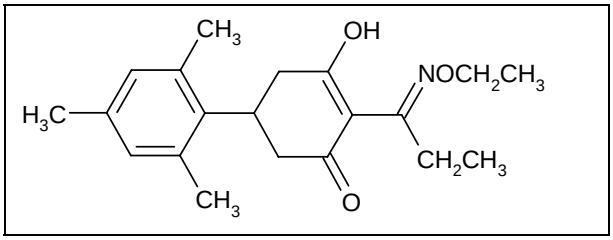
Rapporteur Member State	United Kingdom
Co-rapporteur Member State	-

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	(*RS*)-2-[(*EZ*)-1-(ethoxyimino)propyl]-3-hydroxy-5-mesitylcyclohex-2-en-1-one
Chemical name (CA) ‡	2-[1-(ethoxyimino)propyl]-3-hydroxy-5-(2,4,6-trimethyl phenyl)-2-cyclohexen-1-one
CIPAC No ‡	544
CAS No ‡	87820-88-0
EC No (EINECS or ELINCS) ‡	Not available
FAO Specification (including year of publication) ‡	None listed
Minimum purity of the active substance as manufactured ‡	Technical concentrate (TK) Minimum purity= 780g/kg Maximum purity= 900 g/kg NB the minimum purity of the technical material (TC) is 960g/kg. The NOT has confirmed that only the TK material is currently manufactured.
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	None
Molecular formula ‡	$C_{20}H_{27}NO_3$
Molecular mass ‡	329.4 g/mol

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

Structural formula ‡



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

Physical and chemical properties (Annex IIA, point 2)

Physical and chemical properties reported here should be interpreted with caution as the E/Z isomer ratio is dependent on the sample environment and the values reported here relate only to the conditions of these specific tests and may vary with varying conditions.

Melting point (state purity) ‡	110.3 °C (99.4 %)
Boiling point (state purity) ‡	Cannot be determined as decomposition begins before the boiling point is reached.
Temperature of decomposition (state purity)	129°C (99.4 %)
Appearance (state purity) ‡	Pure active substance (99.0%): white solid Technical concentrate (81.4%): white powder
Vapour pressure (state temperature, state purity) ‡	$3.7 \cdot 10^{-10}$ kPa at 20°C (99.0 %)
Henry's law constant ‡	$1.8 \cdot 10^{-5}$ Pa · m^3/mol at pH 5.2 $2.0 \cdot 10^{-5}$ Pa · m^3/mol at pH 6.5, purified water $1.2 \cdot 10^{-5}$ Pa · m^3/mol at pH 9.0
Solubility in water (state temperature, state purity and pH) ‡	6.7mg /L at 22°C (pH 5.2) (99.0%) 6.1mg /L at 22°C (pH 6.5) (99.0%) 9820 mg /L at 22°C (pH 9.0) (99%)
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 24°C in g/L (92.4%) Acetone 89 g/l Dichloromethane > 500 g/l Ethyl acetate 110 g/l Hexane 18 g/l Methanol 25 g/l Toluene 213 g/l
Surface tension ‡ (state concentration and temperature, state purity)	53 mN/m at 20 °C (90 % saturated solution, 81.4% purity)
Partition co-efficient ‡ (state temperature, pH and purity)	log $P_{O/W}$ = 2.1 at 20 °C (ASTM Type II water. ASTM spec. suggests pH ≤7) (99.0% purity) No data on effect of pH. However, as degree of ionisation increases with pH, log P_{OW} is expected to decrease with increasing pH.
Dissociation constant (state purity) ‡	pKa = 4.3 at 25°C (99.0%)

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

UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	neutral, methanol solution: λ_{max} (nm); ε ($L.mol^{-1}.cm^{-1}$) 220; 16454 258; 11500 285; 10347 310; 2569 No value of ε at 290nm. Estimated from spectrum as 9438 l/mol.cm. acidic, 90:10 methanol :1N HCl 220; 16518 258; 13577 310; 3156 No value of ε at 290nm. Estimated from spectrum as 5525 l/mol.cm. basic, 90:10 methanol :1N NaOH 220; 15577 283; 23583 310; 886 No value of ε at 290nm. Estimated from spectrum as 20947 l/mol.cm.
Flammability ‡ (state purity)	Not highly flammable. Not classified (81.4%)
Explosive properties ‡ (state purity)	Not classified (81.4%)
Oxidising properties ‡ (state purity)	Not classified (81.4%)

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

Summary of representative uses evaluated (*tralkoxydim*)*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g as/hL min – max (l)	water L/ha min – max	g as/ha min – max (l)		
Wheat (plus rye and triticale) Barley (plus oats)	Southern Europe	Grasp 25SC	F	Weeds	SC	250g/l	Spray	Up to BBCH 32	1	-	110- 150	300 / 400	450	-	[1]

[1] Safe use has not been shown concerning the long term risk to herbivorous mammals, where a higher tier risk assessment is required

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

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

Appendix 1.2 Methods of Analysis

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

Technical as (analytical technique)	HPLC with UV detection
Impurities in technical as (analytical technique)	HPLC with UV detection
Plant protection product (analytical technique)	HPLC with UV detection

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Tralkoxydim
Food of animal origin		Not required
Soil		Tralkoxydim
Water	surface	Tralkoxydim
	drinking/ground	Tralkoxydim and R173642
Air		Tralkoxydim

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	HPLC with single-ion MS/MS detection. LOQ: 0.01mg/kg (tralkoxydim) for wheat straw, wheat grain, orange, tomato, oat forage, oilseed (rape seed).
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not submitted and not required
Soil (analytical technique and LOQ)	HPLC with single-ion MS/MS detection. LOQ: 0.005mg/kg (tralkoxydim)
Water (analytical technique and LOQ)	HPLC with single-ion MS detection. LOQ: 0.05µg/l (tralkoxydim) Confirmation by MS/MS demonstrated at 0.05µg/l (river water, sea water, groundwater and drinking water) Method for R173642: Open
Air (analytical technique and LOQ)	HPLC with single-ion MS/MS detection. LOQ: 0.14 µg/m^3
Body fluids and tissues (analytical technique and LOQ)	Not submitted and not required.

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

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

	RMS/peer review proposal
Active substance	Not classified

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

Appendix 1.3 Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	Rapidly and extensively absorbed. Approximately 29-58% excreted in urine within 24 hours (64-78% biliary excretion within 48 hours with significant re-absorption and excretion in urine).
Distribution ‡	Widespread (highest levels in rat liver and kidneys).
Potential for accumulation ‡	Low based on residue levels in rat tissues at 7 days.
Rate and extent of excretion ‡	Rapidly eliminated in excreta. Approximately 56-80% of radioactivity with 24 hours of dosing.
Metabolism in animals ‡	The main pathway is the oxidation of one of the methyl groups on the phenyl ring to form tralkoxydim alcohol which is further oxidised *via* an intermediary aldehyde metabolite to form tralkoxydim acid.
Toxicologically relevant compounds ‡ (animals and plants)	Parent and tralkoxydim acid
Toxicologically relevant compounds ‡ (environment)	Parent, tralkoxydim acid and metabolite R173642

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	934 mg/kg bw for females	R22
Rat LD_{50} dermal ‡	>2000 mg/kg bw	
Rat LC_{50} inhalation ‡	>3.5 mg/l (nose only, 4 hrs); the highest dose tested.	
Skin irritation ‡	Mild irritant (classification not warranted)	
Eye irritation ‡	Mild irritant (classification not warranted)	
Skin sensitisation ‡	Negative (M & K test)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Dogs:: Liver: increased weight and enzyme activities, fatty change, vacuolation and proliferation of SER. Adrenals: increased weight and vacuolation of the cortex. Testicular effects at higher dose levels. Rats: reduced bw gain, clinical chemistry, reduced kidney weight, increased liver weight.
Relevant oral NOAEL ‡	0.5 mg/kg bw/day (90d and 1y-dog studies). 20.5 mg/kg bw/day(90d-rat)

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

Relevant dermal NOAEL ‡	>1000 mg/kg bw/day (21d-rat)	
Relevant inhalation NOAEL ‡	No data, not required.	

Genotoxicity ‡ (Annex IIA, point 5.4)

	Equivocal results *in vitro* and negative *in vivo;* overall no genotoxic potential

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

Target/critical effect ‡	Rats: enlarged testes; sperm effets; Leydig cell hyperplasia and tubular atrophy; reduced cholesterol levels; retinal atrophy (female rats only); histological alterations in liver; Hamster: reduced body weight; increased liver and testes weight; histological alterations in liver; (no mouse study available because of porphyria)	
Relevant NOAEL ‡	27.8 mg/kg bw/day (80 wk hamster study) 2.3 mg/kg bw/day (2y-rat)	
Carcinogenicity ‡	Rats: increased incidence of Leydig cell tumours. Hamsters: increased incidence of ovarian tumours.	R40

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Reduced body weight gain and food consumption in parental animals and reduced pup weight and smaller total litter weight. Classification is based on adverse effects on gonads in hamster, dog and rat observed in subchronic/chronic studies.	
Relevant parental NOAEL ‡	18.2 mg/kg bw/day	
Relevant reproductive NOAEL ‡	91 mg/kg bw/day	
Relevant offspring NOAEL ‡	18.2 mg/kg bw/day	R62

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

Developmental toxicity

Developmental target / critical effect ‡	Rat: deaths and reduced bodyweight, post-implantation loss (maternal). Skeletal malformations – misshapen vertebrae and delayed ossification (foetal). Rabbit: reduced bodyweight and food intake, abortions (maternal). Reduced number of live foetuses and intrauterine deaths (foetal).	
Relevant maternal NOAEL ‡	Rat: 30 mg/kg bw/day Rabbit: 20 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 1 mg/kg bw/day Rabbit: 20 mg/kg bw/day	R63

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data, not required.
Repeated neurotoxicity ‡	No data, not required.
Delayed neurotoxicity ‡	No data, not required.

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	
Investigations in hamsters (including toxicokinetics)	Evidence for absorption. Effects on liver enzymes and testosterone hydroxylation.
Investigations into hepatic porphyria in mice & summary.	Mechanism established for tralkoxydim-induced porphyria in mice.
Species differences in tralkoxydim-induced hepatic porphyria	Marked species differences with mice shown to be very susceptible compared to other species investigated.
In vitro studies	Clear mechanistic differences between mouse and human hepatocytes and supports the conclusion that tralkoxydim-induced porphyria in mice is not relevant to the human risk assessment
Investigations in primates (including human data)	Indicates that monkeys are not susceptible to tralkoxydim-induced porphyria and that the metabolism of tralkoxydim in humans is similar to the metabolism in experimental animals.
Studies performed on metabolite R173642 [3-(2,4,6-trimethylphenyl) pentanedioic acid]	
Acute oral toxicity in the rat	LD50 value >2000 mg/kg bw (only females tested).
Genotoxicity (standard in-vitro package)	Negative (in all three assays)

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

90-day dietary study in rats	NOAEL of 26.8 mg/kg bw/day based on the increased severity of renal microlithiasis at the next highest dose.

Medical data ‡ (Annex IIA, point 5.9)

Worker monitoring data.	No significant adverse health effects have been reported for workers engaged in the manufacture and formulation of tralkoxydim products.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.005 mg/kg bw/day	90-day & 12-month dog studies	100
AOEL ‡	0.005 mg/kg bw/day	90-day & 12-month dog studies	100
ARfD ‡	0.01 mg/kg bw	Rat developmental study	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (Grasp 25SC)	Based on *in vitro* dermal absorption across human epidermis performed with Grasp 40SC. Skin absorption values of 0.1% and 1.5% can be proposed for the concentrate and in-use dilution, respectively.

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Application in cereals* UK POEM % of AOEL (tractor, 0.45 kg a.s./ha, without PPE) 362% (tractor, 0.45 kg.a.s./ha, PPE = gloves during mixing/loading) 340% (tractor, 0.45 kg.a.s./ha, PPE = gloves during mixing/loading and application) 80% German Model % of AOEL (tractor, 0.45 kg a.s./ha, without PPE) 88% (tractor, 0.45 kg a.s./ha, PPE = gloves during mixing/loading) 82% (tractor, 0.45 kg a.s./ha, PPE = gloves during mixing/loading and application) 68%

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

Workers	According to German re-entry exposure model (Hoernicke *et al* 1998) and using EUROPOEM dislodgeable foliar residue and transfer coefficient values: 4.5% of AOEL (no PPE)
Bystanders	According to Lloyd and Bell, 1983: 4% of AOEL

* As a result of 'GRASP 25 SC' carrying the risk phrase '*May cause sensitisation by skin contact*', suitable protective gloves and coveralls are necessary PPE to be worn during mixing and loading operations.

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

	RMS/peer review proposal
Active substance	**R22** Harmful if swallowed **R40** Limited evidence of carcinogenic effect **R62** Possible risk of impaired fertility **R63** Possible risk of harm to the unborn child

‡ 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).
Rotational crops	Leafy (spinach/mustard); root (turnip); legume (soybean/pea); cereal (millet/wheat). Replant intervals: 30, 105, 300 days
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Not determined. Not required due to low residues in grain (<0.01mg/kg).
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not determined. Not required due to low residues in grain (<0.01mg/kg).
Plant residue definition for monitoring	Tralkoxydim sum of isomers
Plant residue definition for risk assessment	Tralkoxydim sum of isomers
Conversion factor (monitoring to risk assessment)	Not required

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

Animals covered	Goat, hen
Time needed to reach a plateau concentration in milk and eggs	5 days in milk 8 days in eggs
Animal residue definition for monitoring	Not required
Animal residue definition for risk assessment	Not required
Conversion factor (monitoring to risk assessment)	Not required
Metabolism in rat and ruminant similar (yes/no)	Discrete differences noted, but none give rise to toxicological concern.
Fat soluble residue: (yes/no)	Not concluded

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

	Not required. Based on hot rotational crop studies residues in succeeding crops are unlikely if tralkoxydim is used according to GAP.

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

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

Stored residue on grain and straw showed acceptable stability on storage (-18°C) for 18 months and 9 months respectively and stored residues on wheat forage showed acceptable stability on storage (-15°C) for 21 months.

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)	No	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)	Residues in tissues <2.8 mg/kg at > 1000N rate therefore residues expected to be <0.01 mg/kg	Residues in tissues <0.566 mg/kg at > 1000N rate therefore residues expected to be <0.01 mg/kg	Not required
	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 residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/ comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Wheat	Mediterranean	4x<0.01 (<0.01 for both grain and straw)	Grain and straw	0.01*	0.01	0.01
Barley	Mediterranean	4x<0.01 (<0.01 for both grain and straw)	Grain and straw	0.01*	0.01	0.01

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

‡ 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	0.005 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	<1%
TMDI (% ADI) according to national (to be specified) diets	2 % (UK)
IEDI (WHO European Diet) (% ADI)	<1%
NEDI (specify diet) (% ADI)	2 % max for toddler, 4-6 and 7-10 yr old children (UK)
Factors included in IEDI and NEDI	Not required
ARfD	0.01 mg/kg bw
IESTI (% ARfD)	-
NESTI (% ARfD) according to national (to be specified) large portion consumption data	< 1% (UK) for child-bearing age populations
Factors included in IESTI and NESTI	Not required

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Not determined. Not required due to low residues in grain (<0.01mg/kg).				

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

Wheat, rye and triticale (grain)	0.01mg/kg*
Barley, oats (grain)	0.01mg/kg*

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

‡ 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 ‡	55.1 % after 94 d, [^{14}C-PH]-label (n = 5) 52.7 % after 90 d, [^{14}C-CH]-label (n = *2*) Sterile conditions: <0.1 % after 90 d (n = 1)
Non-extractable residues after 100 days ‡	44.5 % after 90 d, [^{14}C-PH]-label (n = 5) 29.7 % after 90 d, [^{14}C-CH]-label (n = 2)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	R173642[21] – 17.2 % at 15 d (n = 3) [^{14}C-PH] label R223068 – 12.5 % at 15 d (n = 7) R163434 – 7.5 % at 7 d (n = 7) – present at > 5% AR in two consecutive timepoints [^{14}C-PH] & [^{14}C-CH] labels

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

Anaerobic degradation ‡	
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No study submitted and none required for Southern EU use.
Soil photolysis	
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None (metabolite R163434 present at 11.7% AR in irradiated samples and 27.6% AR in dark controls – therefore presumed to be formed by hydrolysis). The SFO DT50 in the light (corrected for degradation in dark control) = 1.96d of 8h/day irradiation.

[21] R173642 (3-(2,4,6-trimethylphenyl) pentanedioic acid)
R223068 (4-[2-(1-{ethoxyimino}propyl)-3-hydroxy-2-cyclohexene-1-one-5-yl]-3,5-dimethyl benzoic acid)
R163434 (3-ethyl-4,5,6,7-tetrahydro-4-oxo-6-(2,4,6-trimethylphenyl)-1,3-benzoxazole)

‡ 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)

Laboratory studies ‡

Tralkoxydim	Aerobic conditions					
Soil type (USDA)	pH (H_2O)	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam	6.7	20°C / 40 %	2.2 / 7.2	1.2	0.989	SFO
Sandy clay loam	6.9	20°C / 40 %	2.5 / 8.2	1.8	0.987	SFO
Sandy loam	7.9	20°C / 40 %	5.6 / 18.6	2.8	0.997	SFO
Sandy loam	6.5	20°C / 40 %	2.8 / 9.2	1.9	0.995	SFO
Loamy sand	5.7	20°C / 40 %	1.1 / 3.7	0.8	0.980	SFO
Loamy sand	6.4	20°C / 40 %	3.4 / 11.1	2.6	0.731	SFO
Sandy loam	6.5	20°C / 40 %	6.1 / 20.2	4.1	0.870	SFO
Sandy loam	7.0	10°C / 40 %	10.7 / 35.4	3.3	0.974	SFO
Sandy clay loam	6.7	10°C / 40 %	12.2 / 40.6	3.5	0.942	SFO
Loamy sand	8.3	10°C / 40 %	31.0 / 103.0	10.8	0.975	SFO
			Geometric mean/median	2.6 / 2.7		

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

Metabolites

R173642	Aerobic conditions						
Soil type (USDA)	pH (H_2O)	t. °C / % MWHC	Form. Fract.	DT_{50} /DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam	6.7	20°C / 40 %	0.273	13.0 / 43.2	7.1	0.988	SFO
Sandy clay loam	6.9	20°C / 40 %	0.188	12.1 / 40.1	8.6	0.989	SFO
Sandy loam	7.9	20°C / 40 %	0.340	14.0 / 46.3	7.0	0.997	SFO
Sandy loam	7.0	10°C / 40 %	*	79.8 / 265	24.5	0.957	SFO
Sandy clay loam	6.7	10°C / 40 %	*	64.3 / 214	18.3	0.83	SFO
Loamy sand	8.3	10°C / 40 %	*	245.8 / 816	86.1	0.842	SFO
Geometric mean/median			0.27 (arith. Mean)	-	16.0 / 13.5	-	
R223068	Aerobic conditions						
Soil type (USDA)	pH (H_2O)	t. oC / % MWHC	Form. Fract.	DT_{50} /DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam	6.7	20°C / 40 %	0.197	6.3 / 20.9	3.4	0.992	SFO

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

Sandy clay loam	6.9	20°C / 40 %	0.293	2.0 / 6.6	1.4	0.991	SFO
Sandy loam	7.9	20°C / 40 %	0.163	17.1 / 56.9	8.6	0.996	SFO
Sandy loam	6.5	20°C / 40 %	0.227	5.2 / 17.2	3.5	0.994	SFO
Loamy sand	5.7	20°C / 40 %	0.086	13.7 / 45.6	10.5	0.978	SFO
Sandy loam	7.0	10°C / 40 %	*	13.0 / 43.2	4.0	0.992	SFO
Sandy clay loam	6.7	10°C / 40 %	*	5.0 / 16.5	1.4	0.996	SFO
Loamy sand	8.3	10°C / 40 %	*	49.2 / 163.5	17.2	0.969	SFO
Geometric mean/median			0.19 (arith. Mean)	-	4.4 / 3.8	-	
R163434	Aerobic conditions						
Soil type (USDA)	pH (H_2O)	t. °C / % MWHC	Form. Fract.	DT_{50} /DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam	6.7	20°C / 40 %	0.10	25.1 / 83.5	13.7	0.99	SFO
Sandy clay loam	6.9	20°C / 40 %	0.085	18.7 / 62.2	13.3	0.99	SFO
Sandy loam	7.9	20°C / 40 %	0.209	2.4 / 7.8	1.2	1.00	SFO
Sandy loam	6.5	20°C / 40 %	0.058	19.2 / 63.9	12.9	0.99	SFO

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

Loamy sand	5.7	20°C / 40 %	0.069	40.9 / 135.8	31.4	0.98	SFO
Geometric mean/median			0.10 (arith. Mean)		9.8 / 13.3	-	

*studies performed with metabolite as starting material therefore no formation fraction derived.

Field studies

None submitted and none required (Note field studies representative of Northern EU use may be available)

pH dependence (yes / no) (if yes type of dependence) ‡	No clear correlation although some evidence of slower degradation of tralkoxydim at increasing soil pH. Mean/median soil DT50 values may be used for ground and surface water exposure assessments.

Soil accumulation and plateau concentration ‡	Not required

Soil adsorption/desorption (Annex IIA, point 7.1.2)
Tralkoxydim

Soil Type (USDA)	OM %	Soil pH (H_2O)	Kd	Kf	Koc	Kfoc	1/n
Coarse sand	0.77	5.4	1.4	1.3	314	290	-
Loamy sand	1.9	6.3	1.3	0.81	120	74	-
Sandy loam	2.6	6.5	1.5	0.98	100	65	-
Clay	5.4	6.8	1.1	0.95	35	30	-
Loamy sand	0.5	6.8	0.15	0.16	51	55	1.1
Silty clay loam	3.7	6.2	2.2	2.2	100	100	0.98
				mean/median	Not valid since pH dependence observed		
			pH dependence, Yes or No		Yes: Adsorption inversely related to soil pH		

R173642

Soil Type (USDA)	OM %	Soil pH (H_2O)	Kd	Kf	Koc	Kfoc	1/n
Silty clay loam	3.7	6.2	1.3	1.0	61	48	0.86
Sandy loam	3.1	7.4	0.08	0.05	4.4	3.0	0.75

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

Silty clay loam	3.9	5.7	4.9	3.5	220	150	0.87
Sand	1.0	5.1	1.5	1.21	250	210	0.89
Sandy loam	5.1	8.5	0.13	0.12	4.3	4.2	0.97
				mean/median	Not valid since pH dependence observed		
		pH dependence, Yes or No	Yes: Adsorption inversely related to soil pH				

R223068

Soil Type (USDA)	OM %	Soil pH (H_2O)	Kd	Kf	Koc	Kfoc	1/n
Silty clay loam	3.7	6.2	0.73	0.53	34	25	0.83
Silty clay loam	3.9	5.7	1.4	1.1	62	48	0.87
Sand	1.0	5.1	2.6	2.1	450	360	0.80
Sandy loam	5.1	8.5	0.05	0.06	1.9	2.1	1.22
				mean/median	Not valid since pH dependence observed		
		pH dependence, Yes or No	Yes: Adsorption inversely related to soil pH				

R163434

Soil Type (USDA)	OC %	Soil pH (H_2O)	Kd	Kf	Koc	Kfoc	1/n
Silty loam	0.3	5.3	4.21	2.55	1397	846	0.75
Silty clay	2.0	5.6	24.3	14.2	1216	711	0.81
Silty clay loam	2.5	5.3	12.5	7.48	498	299	0.80
Sandy loam	1.2	6.7	9.93	6.08	828	506	0.79
Sandy clay loam	2.9	6.4	16.7	10.3	576	354	0.83
Loamy sand	1.7	7.8	8.97	5.59	527	329	0.79
				mean/median	840 / 702	508 / 430	0.80 / 0.80
		pH dependence, Yes or No	No				

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

Column leaching	Elution (mm): 660 mm Time period (d): 3 d ageing of residues, 9 weeks elution
	Leachate: 4.7 to 6.7% AR for a loamy sand and a sandy loam soil column No single component represented >0.7% AR
Lysimeter/ field leaching studies ‡	None submitted and none required

‡ 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	DT_{50} (d): 14.1 d Kinetics: single first order Field or Lab: longest laboratory DT50 corrected to 20°C
Application data	Crop: winter or spring cereals Depth of soil layer: 5 cm % plant interception: 0% interception as worst case Number of applications: 1 Application rate(s): 450 g as/ha

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average
Initial	0.600	-
Short term		
24h	0.571	0.585
2d	0.544	0.571
4d	0.493	0.545
Long term		
7d	0.425	0.508
28d	0.151	0.326
56d	0.038	0.204
100d	0.004	0.121

Metabolite R173642

Method of calculation	Molecular weight relative to the parent: 250.3 g/mol (R173642); 329.4 g/mol (tralkoxydim) DT_{50} (d): 112.1 days Kinetics: single first order Field or Lab: longest laboratory DT50 corrected to 20°C
Application data	Application rate assumed: 450 g as/ha (assumed R173642 is formed at a maximum of 17.2 % of the applied dose)

$PEC_{(s)}$ (mg/kg)	Single application Actual
Maximum predicted	0.079

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

Metabolite R223068 Method of calculation	Molecular weight relative to the parent: 359.4 g/mol (R223068); 329.4 g/mol (tralkoxydim) DT_{50} (d): 22.4 days Kinetics: single first order Field or Lab: longest laboratory DT50 corrected to 20°C
Application data	Application rate assumed: 450 g as/ha (assumed R223068 is formed at a maximum of 12.5 % of the applied dose)

$PEC_{(s)}$ (mg/kg)	Single application Actual
Maximum predicted	0.082

Metabolite R163434 Method of calculation	Molecular weight relative to the parent: 283 g/mol (R223068); 329.4 g/mol (tralkoxydim) DT_{50} (d): 41 days Kinetics: single first order Field or Lab: longest laboratory DT50
Application data	Application rate assumed: 450 g as/ha (assumed R163434 is formed at a maximum of 7.5 % of the applied dose)

$PEC_{(s)}$ (mg/kg)	Single application Actual
Maximum predicted	0.039

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

Hydrolytic degradation of the active substance and metabolites > 10%.	pH 5: 9.0 d at 25°C(1st order, r^2= 0.96) R163434: 76.8% AR (28 d)
	pH 7: 140 d at 25°C (1st order) R163434 + unknown metabolite 7.0%AR (28 d)
	pH 9: No significant degradation
Photolytic degradation of active substance and metabolites above 10%	Natural summer sunlight, Florida, US, 25-35°N; DT_{50} 5.8 days R159368[22], 22% AR R158378, 22% AR
Quantum yield of direct phototransformation in water at Σ > 290 nm	0.0081 at pH 4 and 0.0051 at pH 9 Average half-life in surface waters of Central Europe in May calculated to be 490 d at pH 7.

[22] R159368 (3-hydroxy-2-propionyl-5-(2,4,6-trimethylphenyl)cyclohex-2-enone)
R158378 (3-hydroxy-2-(1-iminopropyl)-5-(2,4,6-trimethylphenyl)cyclohex-2-enone)

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

Readily biodegradable (yes/no)	No data submitted, substance considered not ready biodegradable.

Degradation in water / sediment

Parent	Distribution (eg max in water 94.2% after 0 d. Max. sed 19.7% after 28 d)								
Water / sediment system	pH w	pH sed	t. °C	DT_{50} whole	St. (r^2)	DT_{50} water	St. (r^2)	DT_{50}- DT_{90} sed	Method of calculation
Virginia Water	7.9-8.0	6.6	20	60.1	>0.9	43.9	>0.9	Not determined	SFO
Dakota Water	8.0-8.3	8.0	20	161.3	>0.9	92.9	>0.9		SFO

Metabolite R158378	Distribution (max in water 5.9% AR after 70d. Max. sed 33.6% AR after 100d)				
Mineralization and non extractable residues					
Water / sediment system	pH w	pH sed	Mineralization	Non-extractable residues in sed. (peak)	Non-extractable residues in sed. (end of the study)
Virginia Water	7.93	6.6	5.8% at end of study (135 d)	20.2% after 100 d	12.8% at end of study (135 d)
Dakota Water	8.05	8.0	2.1% at end of study (135 d)	20.9 after 100 d	14.2% at end of study (135 d)

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

Parent	
Parameters used in FOCUSsw step 1 and 2	Molecular weight: 329.4 g/mol Water solubility: 6.7 mg/l Koc: 30 or 290 ml/g (for maximum PECsw and maximum PECsed respectively) DT_{50} soil (d): 2.7 days (Lab. In accordance with FOCUS SFO) DT50 water/sediment system (d): 161.3 d

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

	(representative worst case from sediment water studies) DT50 water (d): 161.3 d DT50 sediment (d): 161.3 d Crop interception (%): 0% assumed as worst case
Parameters used in FOCUSsw step 3 (if performed)	Vapour pressure: 0 Pa (worst case) Koc: D1: 23.3ml/g R1: 20.2ml/g D2: 30.8ml/g R3: 8.7ml/g D3: 333.2ml/g R4: 4.3ml/g D4: 35.4ml/g D5: 62.0ml/g D6: 15.3ml/g 1/n: 1.0
Application rate	Crop: winter and spring cereals Crop interception: FOCUS Default at Step 3 Number of applications: 1 Application rate(s): 450 g as/ha Aplication window: Julian day 74 to 104
Main routes of entry	2.759% drift from 1 metre 10 % runoff/drainage (at FOCUSsw Step 1) 4 % runoff/drainage (at FOCUSsw Step 2)

Step 1 and 2

Use	Maximum PECsw (µg/l)	Maximum PECsed (µg/kg dry weight)
Tralkoxydim		
Step 1	148.37	320.97
Step 2	24.62	53.22

Step 3 (Only Step 3 scenarios where peak concentration is in excess of Step 2)

Scenario	Maximum PECsw (µg/l)	Maximum PECsed (µg/kg dry weight)
Spring cereals		
D1 ditch	29.1	10.1
Winter cereals		
D1 ditch	32.3	12.2
D2 ditch	45.6	7.7
D2 stream	29.1	4.4

Metabolites

Parameter	Tralkoxydim	R158378	R159368	R173642	R223068	R163434
Mol wt. (g/mol)	329.4	285.4	286.4	250.3	359.4	283
Water solubility (mg/l)	6.7	1000*	1000*	1000*	1000*	1000*
Max. observed in soil studies (%)	-	4.5	0	17.2	12.5	7.5
Max. observed in	-	37.3	22**	6.7	1	3.1

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

water/sediment studies		22**				
Range of K_{foc} (ml/g)	30-290	10,000***	10***	0-210	0-360	430
DT_{50} soil (d)	2.7	300***	-	13.5	3.8	41
DT_{50} water/ sediment (d)	161.3	1000*	1000*	1000*	1000*	1000*
DT_{50} water (d)	161.3	1000*	1000*	1000*	1000*	1000*
DT_{50} sediment (d)	161.3	1000*	1000*	1000*	1000*	1000*

*worst case assumption
**assumed for formation via photolysis
***default according to the Aquatic Guidance Document (for metabolite R158378 a Kfoc value of 10,000ml/g only was assumed since this metabolite was only found in major (>10% AR) amounts in the sediment phase of the water sediment system. For metabolite R159368 a kfoc value of 10 ml/g was assumed since this metabolite was only found in major (>10% AR) amounts in the aqueous photolysis study).

Use	Maximum PECsw (µg/l)	Maximum PECsed (µg/kg dry weight)
R158378		
Step 1	**RMS**: 28.3	50.10
Step 2	**RMS**: 4.7	25.46
R159368		
Step 1	**RMS**: 28.3	-
Step 2	**RMS**: 4.7	-
Step 3	**EFSA**: 8.7	
R173642		
Step 1	19.82	32.49
Step 2	6.60	10.81
R223068		
Step 1	20.50	49.84
Step 2	3.99	9.70
R163434		
Step 1	6.26	26.7
Step 2	2.38	10.2

Maximum PECsw predicted with minimum K_{foc} value
Maximum PECsed predicted with maximum K_{foc} value

Step 3 metabolite R159368
The maximum PECsw value for R159368 at Step 3 would be 8.7µg/l based on simple direct conversion from the peak of tralkoxydim of 45.6µg/l at this scenario. The PECsw value at the next worst case Step 3 scenario (D1 ditch, winter cereals) would be 6.2µg/l. The PEC values are based on maximum drainflow levels entering drainage ditches in the autumn following applications to winter cereals, therefore the assumption that this level of photolysis will occur is considered to be very worst case in southern Europe, particularly for those scenarios that are considered not to be representative of conditions occurring in Southern EU.

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

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUS gw modelling, values used – Modelling using FOCUS model(s), with appropriate FOCUS gw scenarios, according to FOCUS guidance. Model(s) used: FOCUS PELMO (v3.3.2) Scenarios (list of names): All 9 FOCUS scenarios Crop: winter and spring cereals Median parent DT_{50lab} 2.7 d Median R173642 DT_{50lab} 13.5 d Median R223068 DT_{50lab} 3.8 d Median R173642 DT_{50lab} 13.5 d Geometric mean R163434 DT_{50lab} 9.8 d All the above normalised to 10kPa or pF2, 20°C with Q10 of 2.2. Formation fraction R173642 from tralkoxydim: 0.27 Formation fraction R223068 from tralkoxydim: 0.19 Formation fraction R163434 from tralkoxydim: 0.10
Application rate	Application rate: 450 g/ha, 25% crop interception No. of applications: 1 Time of application (month or season): Spring (30th March)

	Soil pH (H_2O)	Tralkoxydim calculated K_{foc} (ml/g)	R173642 calculated K_{foc} (ml/g)	R223068 calculated K_{foc} (ml/g)
Linear regression line of $Ln(K_{foc})$ vs pH		$Ln(K_{foc})$ = -1.4012*pH + 13.235 (r2 = 0.93)	$Ln(K_{foc})$ = -1.4883*pH + 13.038 (r2 = 0.90)	$Ln(K_{foc})$ = -1.5719*pH + 13.106 (r2 = 0.87)
Châteaudun	8	7.6[a]	3.1	1.7
Hamburg	6.4	71.3	33.5	21.0
Jokioinen	6.2	94.4	45.2	28.8
Kremsmünster	7.7	11.5[a]	4.8	2.7
Okehampton	5.8	165.3	81.9	54.0
Piacenza	7	30.8[a]	13.7	8.2
Porto	4.9	583.5[a]	312.7[a]	222.2[a]
Sevilla	7.3	20.2[a]	8.8	5.1
Thiva	7.7	11.5[a]	4.8	2.7

[a]: extrapolated beyond the measured laboratory data
1/n for tralkoxydim = 1.0 (data only available for 2 soils and sorption appeared approximately linear over the concentration range tested)
1/n for R173642 = 0.87 (mean of 5 values taken as there was no clear correlation between pH and 1/n)
1/n for R223068 = 0.96 (mean of 4 values taken as there was no clear correlation between pH and 1/n)
Kfoc for R163434 = 430ml/g; 1/n = 0.80

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

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

FOCUS PELMO v 3.3.2

Scenario	Crop	Tralkoxydim PECgw (µg/l)	R173642 PECgw (µg/l)	R223068 PECgw (µg/l)	R163434 PECgw (µg/l)
Châteaudun	Winter cereals	<0.001	0.074	<0.001	<0.001
	Spring cereals	<0.001	0.025	<0.001	<0.001
Hamburg	Winter cereals	<0.001	0.001	<0.001	<0.001
	Spring cereals	<0.001	<0.001	<0.001	<0.001
Jokioinen	Winter cereals	<0.001	<0.001	<0.001	<0.001
	Spring cereals	<0.001	<0.001	<0.001	<0.001
Kremsmünster	Winter cereals	0.001	0.435	0.012	<0.001
	Spring cereals	<0.001	0.279	0.002	<0.001
Okehampton	Winter cereals	<0.001	<0.001	<0.001	<0.001
	Spring cereals	<0.001	<0.001	<0.001	<0.001
Piacenza	Winter cereals	0.008	0.076	0.037	<0.001
Porto	Winter cereals	<0.001	<0.001	<0.001	<0.001
	Spring cereals	<0.001	<0.001	<0.001	<0.001
Sevilla	Winter cereals	<0.001	<0.001	<0.001	<0.001
Thiva	Winter cereals	<0.001	<0.001	<0.001	<0.001

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

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	Not studied - no data requested
Photochemical oxidative degradation in air ‡	DT_{50} of 0.069 d based on an OH radical concentration of 1.5 x 10^6 cm^{-3} on a 12h day basis derived by the Atkinson method of calculation
Volatilisation ‡	No data submitted, non required
Metabolites	None

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

PEC (air)

Method of calculation	Expert judgement

$PEC_{(a)}$

Maximum concentration	Assumed to be negligible

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: tralkoxydim, R173642, R223068, R163434 (>5% at two timepoints) Surface Water:tralkoxydim, R158378 (sediment and aqueous photolysis metabolite), R159368 (photolysis metabolite), R173642 (from soil), R223068 (from soil), R163434 (from soil) Ground water: tralkoxydim, R163434, R173642, R223068 Air: tralkoxydim

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

Soil (indicate location and type of study)	No data provided - none requested
Surface water (indicate location and type of study)	No data provided - none requested
Ground water (indicate location and type of study)	No data provided - none requested
Air (indicate location and type of study)	No data provided - none requested

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

Candidate for R53 (not ready biodegradable)

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

Appendix 1.6 Effects on non target species

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

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
Alectoris rufa	a.s.	Acute	2024	-
Colinus virginianus	a.s.	Short-term	1018	6237 (by calc.n)
Colinus virginianus	a.s.	Long-term	14.3	150
Mammals ‡				
rat	a.s.	Acute	934	-
rat	a.s.	Long-term[1]	18.2[2]	200
rabbit	a.s.	Long-term	20[2]	
Additional higher tier studies - No additional effects data				

[1] 3-generation study.
[2] Long-term endpoint lowered following discussions at PRAPeR 33, see Evaluation Table.

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

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

Tier 1 (Birds)					
Crop	Application rate (kg as/ha)	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
Cereals (early)	0.45	Large herbivorous bird	Acute	72.0	10
Cereals (early and late)	0.45	Small insectivorous bird	Acute	83.2	10
Cereals (early)	0.45	Large herbivorous bird	Short-term dietary	67.6	10
Cereals (early and late)	0.45	Small insectivorous bird	Short-term dietary	75.0	10
Cereals (early)	0.45	Large herbivorous bird	Long-term reproductive	**1.7**	5
Cereals (early and late)	0.45	Small insectivorous bird	Long-term reproductive	**1.1**	5
Higher tier refinement (Birds)					
Cereals (early)	0.45	Large herbivorous bird	Long-term reproductive	11.5[1]	5
Cereals (early and late)	0.45	Small insectivorous bird	Long-term reproductive	7.5[2]	5
Tier 1 (Mammals)					
Cereals (early)	0.45	Small herbivorous mammal	Acute	10.5	10
Cereals (early and late)	0.45	Insectivorous mammal	Acute	235.3	10
Cereals (early and late)	0.45	Insectivorous mammal	Long-term reproductive	12.6	5
Cereals (early)	0.45	Small herbivorous mammal	Long-term reproductive	**0.72**	5
Higher tier refinement (Mammals)					
Currently insufficient refinements have been identified to derive a low long-term risk to small herbivorous mammals based on use of the lower long-term endpoint (see above).					

[1] Refined risk assessment using foliar DT50 for tralkoxydim of 1.2 days derived from residues study instead of default value of 10 days (see Addendum to DAR).

[2] Refined risk assessment based on dietary data (PD) for yellow wagtail from Davies (1977) and DT50 on insects of 10 days (see Addendum to DAR).

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

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Laboratory tests				
Fish *(Lepomis macrochirus)*	a.s. Tralkoxydim (92.4% w/w)	Acute	LC50	>6.1
Invertebrates *(Daphnia magna)*	a.s. Tralkoxydim (97.8% w/w)	Acute	EC50	>175
Algae *(Pseudokirchnerialla subcapitata)*	a.s. Tralkoxydim (90.3% w/w)	Acute	EbC50	>5.1
Aquatic plants *(Lemna gibba)*	a.s. Tralkoxydim (90.3% w/w)	Acute	EbC50	1.0
Fish *(Oncorhynchus mykiss)*	a.s. Tralkoxydim (97.4% w/w)	Chronic	NOEC	4.6
Invertebrates *(Daphnia magna)*	a.s. Tralkoxydim (97.0% w/w)	Chronic	NOEC	2.1
Fish *(Oncorhynchus mykiss)*	preparation '25% SC' 25% tralkoxydim + 'Atlox' adjuvant in ratio 3.5:1.	Acute	LC50	25 a.s.
Invertebrates *(Daphnia magna)*	preparation 'YF 7763B' 250 g/L tralkoxydim SC.	Acute	EC50	163 a.s. [n]
Aquatic higher plants *(Lemna gibba)*	preparation 'A-12706 A' 242 g/L tralkoxydim SC.	Acute	EC50 (based on frond numbers)	22.7 a.s. [n]
Fish *(Oncorhynchus mykiss)*	metabolite R173642	Acute	LC50	>120
Invertebrates *(Daphnia magna)*	metabolite R173642	Acute	EC50	85
Aquatic higher plants *(Lemna gibba)*	metabolite R173642	Acute	EC50 (based on increase in biomass)	99
Fish *(Pimephales promelas)*	metabolite R223068	Acute	LC50	44
Invertebrates *(Daphnia magna)*	metabolite R223068	Acute	EC50	>110
Aquatic higher plants *(Lemna gibba)*	metabolite R223068	Acute	EC50 (based on frond numbers)	53
Invertebrates *(Daphnia magna)*	metabolite R158378	Acute	EC50	>5 [n]
Algae *(Pseudokirchnerialla subcapitata)*	metabolite R158378	Acute	EbC50, ErC50	>5 [n]
Sediment dwellers *(Chironomus riparius)*	metabolite R158378	Chronic	NOEC (based on emergence and development rate)	100 [n] mg/kg dry sediment
Microcosm or mesocosm tests - None submitted				

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

[n] endpoint based on nominal concentrations, all others based on mean measured.

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

FOCUS Step 1 - Cereals at 0.45 kg a.s./ha

Test substance	Organism	Toxicity end point (mg/L)	Time-scale	PEC_i (mg/L)	TER Step 1	Annex VI Trigger
Tralkoxydim	Fish *(Lepomis macrochirus)*	>6.1	Acute	0.148	**>41**	100
Tralkoxydim	Invertebrates *(Daphnia magna)*[1]	>163[1]	Acute	0.148	1101	100
Tralkoxydim	Algae *(Pseudokirchnerialla subcapitata)*	>5.1	Acute	0.148	>34	10
Tralkoxydim	Aquatic higher plants *(Lemna gibba)*	1.0	Acute	0.148	**6.8**	10
Tralkoxydim	Fish *(Oncoryhnchus mykiss)*	4.6	Chronic[2]	0.148	31	10
Tralkoxydim	Invertebrates *(Daphnia magna)*	2.1	Chronic[2]	0.148	14	10
R173642	Fish *(Oncoryhnchus mykiss)*	>120	Acute	0.020	>6000	100
R173642	Invertebrates *(Daphnia magna)*	85	Acute	0.020	4250	100
R173642	Aquatic higher plants *(Lemna gibba)*	99	Acute	0.020	4950	10
R223068	Fish *(Pimephales promelas)*	44	Acute	0.021	2095	100
R223068	Invertebrates *(Daphnia magna)*	>110	Acute	0.021	>5238	100
R223068	Aquatic higher plants *(Lemna gibba)*	53	Acute	0.021	2524	10
R158378	Invertebrates *(Daphnia magna)*	>5	Acute	0.028	>179	100
R158378	Algae *(Pseudokirchnerialla subcapitata)*	>5	Acute	0.028	>179	10
R158378	Sediment dwellers *(Chironomus riparius)*	100	Chronic[2]	0.050 mg/kg dry sediment	2000	10
R159368[3]	Fish *(Lepomis macrochirus)*	>0.61[3]	Acute	0.028	**21.8**	100
R159368[3]	Invertebrates *(Daphnia magna)*[1]	>16.3[3]	Acute	0.028	225	100
R159368[3]	Algae *(Pseudokirchnerialla subcapitata)*	>0.51[3]	Acute	0.028	18.2	10
R163434[3]	Fish *(Lepomis macrochirus)*	>0.61[3]	Acute	0.002	>305[4]	100
R163434[3]	Invertebrates *(Daphnia magna)*[1]	>16.3[3]	Acute	0.002	>8150[4]	100
R163434[3]	Algae *(Pseudokirchnerialla*	>0.51[3]	Acute	0.002	>255[4]	10

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

	subcapitata)					

TERs in **bold** fail the Annex VI trigger and are followed through to FOCUS Step 3 - see below
[1] Using endpoint from plant protection product
[2] Only R158378 predicted to persist in sediment
[3] Minor metabolite, no studies submitted, assumed to be 10x more toxic than parent
[4]TER values calculated by EFSA after the peer review process.

FOCUS Step 3[1] (only those TERs failing Step 1) - Cereals at 0.45 kg a.s./ha

Test substance	Organism	Toxicity end point (mg/L)	Time-scale	PEC_i (mg/L)	TER Step 1	Annex VI Trigger
Tralkoxydim	Fish *(Lepomis macrochirus)*	>6.1	Acute	0.046[2]	>133	100
Tralkoxydim	Aquatic higher plants *(Lemna gibba)*	1.0	Acute	0.046[2]	22	10
R1593683[3]	Fish (Lepomis macrochirus)	>0.613[3]	Acute	0.087[4]	**70**[4]	100

[1] FOCUS Step 3 give higher PECsw values than FOCUS Step 2 and is therefore used in the refined assessment
[2] PECsw for max concentration in D2 ditch
[3] Minor metabolite, no studies submitted, assumed to be 10x more toxic than parent
[4] TER based on max. FOCUS Step 3 PECsw in D2 ditch. At the next highest PECsw for the D1 ditch the TER would be >98.4. All other drainflow and run-off scenarios would pass at Step 3, including the South European scenariso relevant for the representative uses. These TERs are based on the direct transformation of tralkoxydim into R159368 at peak levels in laboratory photolysis studies. The PEC values are also based on maximum drainflow levels entering drainage ditches in the autumn following applications to winter cereals, therefore this level of photolysis is very worst case even in southern Europe where these drainflow scenarios are less relevant. Given that the toxicity endpoints are also 'greater than' values based on 10 x the toxicity of the parent compound, this adds to the very worst case nature of this assessment. In reality the risk to fish from R159368 in all Step 3 scenarios may be considered to be low.

Bioconcentration	Active substance
log P_{ow}	2.1
Bioconcentration factor (BCF)‡	32 (whole fish); 13 (muscle); 185 (viscera)*
Annex VI Trigger for the bioconcentration factor	N/A (log Pow < 3.0)
Clearance time (days) (CT_{50})	1 day (viscera); 3 days (muscle and whole fish)
Level and nature of residues (%) in organisms after the 14 day depuration phase	Not calculated

* based on total ^{14}C

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

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

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
a.s. ‡	-	>100
Preparation: 'A-12706 A' 242 g/L tralkoxydim SC	>117 a.s.	>100 a.s.
Field or semi-field tests - Not required		

Hazard quotients for honeybees (Annex IIIA, point 10.4)

Cereals at 0.45 kg a.s./ha

Test substance	Route	Hazard quotient	Annex VI trigger
a.s.	Contact	<4.5	50
Preparation: 'A-12706 A' 242 g/L tralkoxydim SC	Contact	<4.5	50
Preparation: 'A-12706 A' 242 g/L tralkoxydim SC	oral	<3.8	50

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

Laboratory tests with standard sensitive species

Species	Test substance	End point	Effect (LR_{50} g a.s./ha)
Typhlodromus pyri ‡	'YF 7763B' 252 g a.s./L SC	Mortality	>450
Aphidius rhopalosiphi ‡	'YF 7763B' 252 g a.s./L SC	Mortality	>450

Hazard Quotients for standard sensitive species based on Tier 1 data
Cereals at 0.45 kg a.s./ha

Test substance	Species	Effect (LR50 g a.s./ha)	HQ in-field	HQ off-field	Trigger
'YF 7763B' 252 g a.s./L SC	*Typhlodromus pyri*	>450	<1.0	-	2
'YF 7763B' 252 g a.s./L SC	*Aphidius rhopalosiphi*	>450	<1.0	-	2

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

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Initial dose (g a.s./ha)	End point	% effect	Trigger value
Pterostichus cupreus	Adult	'JF 9492' (236 g a.s./L) SC 6-days, adults on soil	350; 1750	Mortality	0; 0	50 %
Pardosa spp	Adult	'JF 9492' (236 g a.s./L) SC 6-days, adults on soil	350; 1750	Mortality	0; 0	50 %

Field or semi-field tests - Not required

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

Test organism	Test substance	Time scale	End point[1]
Earthworms			
Eisenia fetida	Technical active substance	Acute 14 days	LC50 >1000 mg a.s./kg d.w.soil
Eisenia fetida	Preparation: 'A-12706 A' 242 g/L tralkoxydim SC	Acute 14 days	LC50 >1000 mg a.s./kg d.w.soil
Eisenia fetida	Metabolite: R173642	Acute 14 days	LC50 >1000 mg/kg d.w.soil
Eisenia fetida	Metabolite: R223068	Acute 14 days	LC50 >1000 mg/kg d.w.soil
Soil micro-organisms			
Nitrogen mineralisation	Technical active substance	Not tested	
	Preparation: 'JF9517' 100 g/L tralkoxydim EC	No effects >25% at 2.5 mg a.s./kg dry soil over 0-76 days. Maximum PEC for active substance is 0.6 mg/kg	
	Metabolite: R173642	No effects >25% at 0.39 mg/kg dry soil over 0-28 days Maximum PEC for R173643 is 0.079 mg/kg	
	Metabolite: R223068	No effects >25% at 0.42 mg/kg dry soil over 0-28 days Maximum PEC for R223068 is 0.082 mg/kg	
Carbon mineralisation	Technical active substance	Not tested	
	Preparation: 'JF9517' 100 g/L tralkoxydim EC	No effects >25% at 2.5 mg a.s./kg dry soil over 0-46 days. Maximum PEC for active substance is 0.6 mg/kg	

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

Test organism	Test substance	Time scale	End point[1]
Carbon mineralisation	Metabolite: R173642	No effects >25% at 0.39 mg/kg dry soil over 0-28 days Maximum PEC for R173643 is 0.079 mg/kg	
	Metabolite: R223068	No effects >25%No effects >25% at 0.42 mg/kg dry soil over 0-28 days Maximum PEC for R223068 is 0.082 mg/kg	
Field studies: Not required[2]			

[1] end points **not** corrected due to log P_{ow} (<2.0)
[2] No chronic earthworm or litter bag tests due to soil dissipation rate of tralkoxydim (maximum DT_{90}: 47 days)

Toxicity/exposure ratios for soil organisms

Cereals at 0.45 kg a.s./ha

Test organism	Test substance	Time scale	Initial soil PEC	TER	Trigger
Earthworms					
Eisenia fetida	a.s. ‡	Acute	0.600	>1667	10
Eisenia fetida	Preparation	Acute	0.600	>1667	10
Eisenia fetida	Metabolite: R173642	Acute	0.079	>12658	10
Eisenia fetida	Metabolite: R223068	Acute	0.082	>12195	10

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

Laboratory dose:response tests. Cereals at 0.45 kg a.s./ha

Most sensitive species	Test substance	ER_{50} (g a.s./ha) vegetative vigour	ER_{50} (g a.s./ha) pre-emergence	Exposure[1] (g a.s /ha)	TER	Trigger
Zea Mays	'Achieve' 80% tralkoxydim WG	32 (shoot length)	-	12.45	1 m: **2.6** 5 m: 12.5	5
Lolium perenne	'Achieve' 80% tralkoxydim WG	-	180 (shoot dry weight)		1 m: 14.5	5

[1] Exposure based on standard Ganzelmeier & Rautmann drift data at 1 and 5 m

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

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

Test type/organism	End point
Activated sludge	tralkoxydim technical: 3 hour EC_{50}: >100 mg/L

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

Compartment	
soil	Parent (tralkoxydim), Metabolites (R173642, R223068)
water	Parent (tralkoxydim), Metabolites (R173642, R223068, R158378, R159378)
sediment	Metabolite R153378
groundwater	Parent (tralkoxydim), Metabolites (R173642, R223068, R163434)

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

	RMS/peer review proposal
Active substance	N R51/53 Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment S61 Avoid release to the environment

	RMS/peer review proposal
Preparation	R52/53 Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment S57 Use appropriate container to avoid environmental contamination

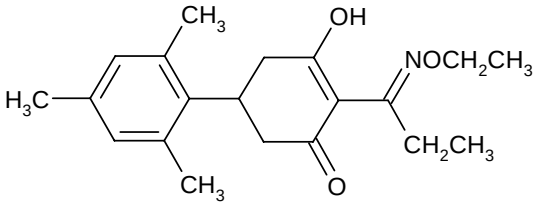
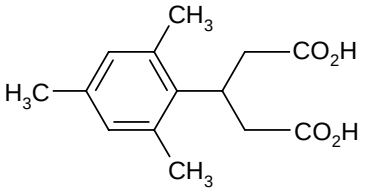
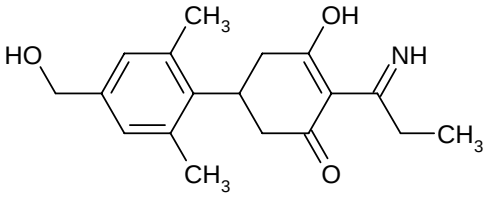
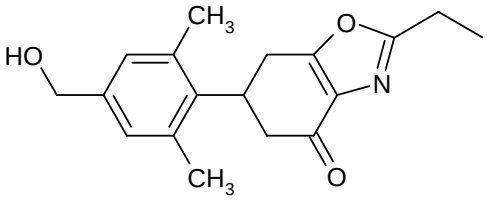
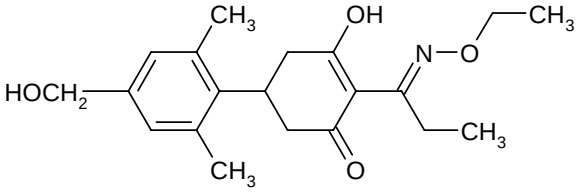
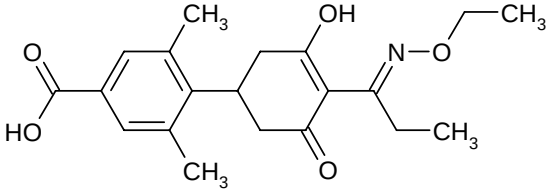
‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

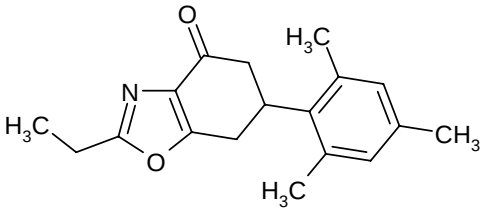
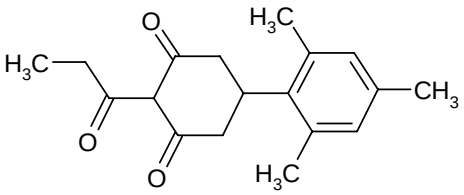
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
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

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
Tralkoxydim	2-[1-(ethoxyimino)propyl]-3-hydroxy-5-mesitylcyclohex-2-enone	
R173642	3-(2,4,6-trimethylphenyl)pentanedioic acid	
R400307	3-hydroxy-2-(imino-1-propyl)-5-dimethyl-4-hydroxymethylphenyl)cyclohex-2-enone	
R237434	2,6-dimethyl-4-(2-ethyl-4,5,6,7-tetrahydrobenzoxazol-4-one)benzyl alcohol	
R209490	3,5-dimethyl-4-(2-[1-(ethoxyimino)propyl]-3-hydroxycyclohex-2-enone-S-yl)benzyl alcohol	
R223068	4-[2-(1-{ethoxyimino}propyl)-3-hydroxy-2-cyclohexene-1-one-5-yl]-3,5-dimethyl benzoic acid	

Appendix 3 – used compound code(s)

Code/Trivial name	Chemical name	Structural formula
R163434	2-ethyl-4,5,6,7-tetrahydro-4-oxo-6-(2,4,6-trimethylphenyl)benzoxazole	
R159368	3-hydroxy-2-propionyl-5-(2,4,6-trimethylphenyl)cyclohex-2-enone	
R158378	3-hydroxy-2-(1-iminopropyl)-5-(2,4,6-trimethylphenyl)cyclohex-2-enone