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

Sulcotrione

Finalised: 31 July 2008

SUMMARY

Sulcotrione is one of the 84 substances of the third stage Part B 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 six months a conclusion on the risk assessment to the EU-Commission.

Germany being the designated rapporteur Member State submitted the DAR on sulcotrione in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 9 August 2006. The peer review was initiated on 15 September 2006 by dispatching the DAR for consultation of the Member States and the sole applicant Bayer CropScience AG. Subsequently, the comments received on the DAR were examined and responded to by the rapporteur Member State in the reporting table. This table was evaluated by EFSA to identify the remaining issues. The identified issues as well as further information made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in March – April 2008.

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

The conclusion was reached on the basis of the evaluation of the representative use as a herbicide on maize. Full details of the GAP can be found in the attached list of end points.

The representative formulated product for the evaluation was "Mikado", a suspension concentrate (SC).

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

Adequate methods are available to monitor all compounds given in the respective residue definition. Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues. It is noted that the residue definitions for soil and water are not yet finalised.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that some quality control measurements of the plant protection product are possible. Data gaps have been identified for the specification, and for a new method of analysis for sulcotrione in air.

In the mammalian metabolism studies, sulcotrione was rapidly and completely absorbed and excreted after oral administration. It was poorly distributed into tissues and organs, and metabolism was limited. The acute toxicity of sulcotrione was low, either by the oral, dermal or inhalation route. It did not present eye or skin irritation properties; however, it was proposed to classify the active substance with risk phrase R43 "may cause sensitisation by skin contact" as a high rate of sensitisation was observed in a Magnusson & Kligman test.
Sulcotrione is a 4-hydroxyphenylpyruvate dioxygenase (HPPD) inhibitor, a key enzyme of the tyrosine catabolic pathway, resulting in increased 4-hydroxyphenyl pyruvate, the proximal tyrosine metabolite and increased blood tyrosine concentration. Male rats were recognised as being more sensitive to sulcotrione and primary effects in short term and long term studies were characterized by corneal lesions and increased liver and kidney weights associated with histopathological findings. Corneal lesions have been shown to be irrelevant for human risk assessment, but liver and mainly kidney effects were considered as sulcotrione-mediated effects (opposed to tyrosinaemia-related effects) and relevant for human risk assessment. The relevant NOAEL for short term exposure was the dose level of 3.3 mg/kg bw/day from the 90-day rat study, while after long term exposure, only a LOAEL could be determined, at 0.04 mg/kg bw/day from the 2-year rat study.
Inconsistent results were obtained from genotoxicity studies, some positive *in vitro* tests were obtained as well as one out of three *in vivo* micronucleus assays. Higher relevance was given to a negative *in vivo* UDS assay and it was concluded, based on the weight of evidence, that sulcotrione had no genotoxic potential *in vivo*. No potential for carcinogenicity was found either.
Reproduction toxicity studies reflected the same effects in parents, but abnormalities of the urinary tract were increased in pups of both generations, not observed in the first parental animals, and on this basis, a classification with Xn, R63 "possible risk of harm to the unborn child" was proposed. The relevant NOAEL (parental) was the dose level of 0.06 mg/kg bw/day, while offspring's NOAEL was 0.6 mg/kg bw/day, no effect on the reproduction or fertility was observed. No developmental effects were observed in either rats or rabbits when sulcotrione was administered by oral gavage and no neurotoxicity was attributed to sulcotrione administration.
A data package of studies was provided on the metabolite CMBA[2], a significant metabolite in plant and the environment, but found only in traces in mammalian metabolism. CMBA was found to be severely irritant to eyes, where it is predominantly formed, at least in the rat, but it did not cause

[2] CMBA: 2-chloro-4-(methylsulfonyl)-benzoic acid

tyrosinaemia and showed to be less toxic than the parent compound. An ADI of 0.2 mg/kg bw/day was set for the metabolite and no relevance was attributed when found in groundwater, even above the threshold value of 0.1 µg/L.
The Acceptable Daily Intake (ADI) of sulcotrione was 0.0004 mg/kg bw/day, the Acceptable Operator Exposure (AOEL) was 0.0006 mg/kg bw/day and no Acute Reference Dose (ARfD) was allocated. Dermal absorption was 0.1 % for the concentrate formulation and 0.5 % for the in-use spray dilution, based on an *in vitro* dermal penetration study through human epidermis. The level of operator exposure calculated for the representative formulation Mikado, at a maximum dose rate of 0.45kg sulcotrione/ha exceeded the AOEL according to the UK POEM, even when the use of personal protective equipment (PPE) was considered; according to the German model, estimated exposure was below the AOEL if PPE as gloves during mixing/loading and application, and coverall and sturdy footwear during application were worn. Estimated exposure of workers entering crops treated with sulcotrione was below the AOEL, even when no PPE was considered. Bystander's exposure was low compared to the AOEL value.

The metabolism of sulcotrione in maize was investigated after post emergence application reflecting the representative use supported by the applicant. The metabolic degradation of sulcotrione is essentially focused to the cyclohexanedione ring and the formation of CMBA. CMBA was the only significant metabolite formed and only occurs at significant levels in the forage. The meeting of experts PRAPeR 45 agreed that it should be included in the residue definition for risk assessment. However, the animal metabolism study where CMBA was dosed showed that no significant residues will occur. Therefore the risk assessment would not have changed except that the ADI has been lowered. Revised TMDI calculations showed intakes at 31 % of the ADI. As CMBA is a significant but non relevant metabolite in ground water at a level above 0.75 µg/L a consumer risk assessment is required. The risk assessment for CMBA gives a highest intake of <0.2 % of the ADI for CMBA.
An acute risk assessment was not necessary as no ARfD has been set.

In soil under aerobic conditions sulcotrione exhibits moderate to medium persistence. Mineralisation of the phenyl ring to carbon dioxide accounted for 2.5-73.8 % applied radioactivity (AR) after 120 days. The formation of unextractable residues was a sink, accounting up to 26.5 % AR after 120 days. The major metabolite CMBA was detected in soil at maximum level of 60% AR. Sulcotrione and CMBA exhibit very high mobility in soil. Adsorption of sulcotrione is not only determined by the organic carbon content of the soil but at least also by the pH value, which itself correlated to the organic carbon content. There was no evidence of a correlation of adsorption with soil pH.
In dark natural sediment water systems sulcotrione degraded exhibiting moderate persistence in the whole system forming the metabolite CMBA (max. 42.2% AR in water and max. 18.6% AR in sediment). The final products of degradation in water-sediment systems were carbon dioxide and bound residues (max 6 and 9% AR after 100 days). The necessary surface water and sediment exposure assessments were appropriately carried out using the agreed FOCUS scenarios approach for sulcotrione at steps 1-3. For the metabolite CMBA appropriate FOCUS step 1 and 2 calculations were carried out. These values are the basis for the risk assessment discussed in this conclusion.

The potential for groundwater exposure from the applied for intended uses by sulcotrione above the parametric drinking water limit of 0.1 µg/L, was concluded to be low for geoclimatic situations that are represented by all pertinent FOCUS groundwater scenarios. CMBA concentrations (80^{th} percentile annual average concentration at 1 m) are in the range of 0.015 – 1.462 µg/L. The concentration of 0.1 µg/L is exceeded in 6 out of 8 European FOCUS scenarios parameterised for maize and for Hamburg and Okehampton scenarios the estimated PEC_{gw} are > 0.75 µg/L. The toxicological assessment was able to conclude that CMBA is not relevant regarding groundwater at the expected concentrations.

As the fate and behaviour of sulcotrione in the environment was investigated using phenyl-labelled sulcotrione only, the peer review process identified a data gap for an aerobic soil degradation study and for a water-sediment study performed with cyclohexanedione-labelled sulcotrione or for evidence to demonstrate that potential metabolites containing the cyclohexanedione ring are labile.

Sulcotrione is not expected to be transferred to the atmospheric compartment and potential for long range transport may be considered negligible.

The first tier acute and short-term TERs for birds and the acute TERs for mammals were above the Annex VI trigger of 10. The first-tier long-term TERs were below the trigger of 5 indicating a potential high long-term risk. The refined risk assessment for medium herbivorous birds resulted in TERs >5 based on residue decline. The experts rejected the suggested PT refinements for insectivorous birds since they were not sufficiently supported by data. A data gap was identified in the expert meeting for the applicant to provide a new refined long-term risk assessment for insectivorous birds. A new study was submitted by the applicant and a refined risk assessment based on this study was included by the RMS in the not peer-reviewed addendum 3 from May 2008. The long-term risk to mammals was refined by using residue decline data and the new (higher) long-term endpoint agreed in the experts meeting. Based on the agreed refinements (without PT refinement) the long-term TERs were above the trigger of 5 indicating a low long-term risk to mammals. The risk from uptake of contaminated drinking water and the risk from the major plant metabolite CMBA to birds and mammals were assessed as low.

Sulcotrione is of low acute toxicity to fish and aquatic invertebrates. The lowest endpoint was observed for aquatic plants. The TERs for all groups of aquatic organisms were greater than the Annex VI triggers of 100 and 10 except for *Lemna gibba*. One (R4 stream) out of seven FOCUS step 3 scenarios resulted in a TER <10 for *Lemna gibba*. Risk mitigation measures are required under environmental conditions represented by scenario R4. The metabolite CMBA is of low toxicity to aquatic organisms including *Lemna gibba*. The Annex VI triggers were exceeded with FOCUS step2 PECsw values.

The risk to the standard non-target arthropod indicator species *Aphidius rhopalosiphi* and *Typhlodromus pyri* was assessed as low. Additional species were tested and no effects of >50% were observed in tests with *Poecilus cupreus* and *Aleochara bilineata*. Effects of >50% were observed in tests with *Coccinella septempunctata* and *Pardosa sp* at the suggested application rate of 450g sulcotrione/ha. The risk to *C. septempunctata* was assessed as low in higher tier (extended laboratory) studies. Several extended laboratory studies were conducted with *Pardosa sp*. After 42 days of ageing

the residues still led to a statistically significantly increased mortality. No increased mortality was observed after 56 days of ageing of residues. Although the effects were <50% it is uncertain if recolonisation would occur in a real field situation due to the long persistence of effects. No further information was made available to demonstrate recovery/recolonisation of spiders in the in-field area. The LR_{50} for *Pardosa sp*. was calculated as 10.34g a.s./ha which is below the calculated off-field exposure rate of 12.47g a.s./ha indicating a potential high risk for spiders in the off-field area. It was agreed by the experts that risk mitigation measures comparable to a 5m in-field no-spray buffer zone should be applied to ensure that recolonisation of the in-field area is possible from unaffected off-field areas. A potential high risk was identified for non-target plants in the off-field area. Risk mitigation measures comparable to a no-spray buffer zone of 10m is recommended.
The risk to bees, earthworms, soil non-target macro- and micro-organisms and biological methods of sewage treatment were assessed as low for the representative use in maize.

Key words: sulcotrione, 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 as amended by Commission Regulation (EC) No 1095/2007, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Sulcotrione is one of the 84 substances of the third stage Part B covered by the Regulation (EC) No 1490/2002 designating Germany as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, Germany submitted the report of its initial evaluation of the dossier on sulcotrione, hereafter referred to as the draft assessment report, received by the EFSA on 9 August 2006. The draft assessment report was distributed for consultation in accordance with Article 11(2) of the Regulation (EC) No 1490/2002 on 15 September 2006 to the Member States and the main applicant Bayer CropScience AG 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, EFSA identified and agreed on lacking information to be addressed by the applicant as well as issues for further detailed discussion at expert level.

Taking into account the requested information received from the applicant, a scientific discussion took place in expert meetings in March – April 2008. 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 on July 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 Panel on Plant Protection Products and their Residues (PPR).

In accordance with Article 11c(1) of the amended 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 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 28 January 2008)
- the consultation report

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

- the reports of the scientific expert consultation
- the evaluation table (rev. 2-1 of 31 July 2008)

Given the importance of the draft assessment report including its addendum (compiled version of June 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

Sulcotrione is the ISO common name for 2-(2-chloro-4-mesylbenzoyl)cyclohexane-1,3-dione (IUPAC).

Sulcotrione belongs to the class of benzoylcyclohexanedione herbicides, other examples of pesticides in this group would be mesotrione and tefuryltrione. Sulcotrione is a hydroxyphenyl pyruvate dioxygenase inhibitor. It is absorbed predominantly by the leaves, but also by the roots.

The representative formulated product for the evaluation was "Mikado", a suspension concentrate (SC).

The evaluated representative use is as a post emergence herbicide on maize. Full details of the GAP can be found in the attached list of end points.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of sulcotrione as manufactured should not be less than 950 g/kg on a dry weight basis. The actual material produced and used in the formulated product is a water wet paste TK the minimum content of sulcotrione in the TK is 630 g/kg but the maximum content has not been provided and a data gap has been identified. It was considered by the meeting of experts PRAPeR 41 that further information was required on the impurity profile of the TK because it was considered that other volatile components may have been present but were lost when the TK was dried down to the TC for analysis. It was also considered that the content of some identified volatile impurities was

actually higher because of losses during drying. Of course the main volatile components were analysed in the TK but the meeting considered other volatile impurities may have been present. A data gap was identified to address this. Since this further information/data is not available the technical specification as a whole should remain provisional.

The technical material contains toluene and hydrogen cyanide, which have to be regarded as relevant impurities. The maximum contents in the technical material on a dry weight basis should not be higher than 80 mg/kg for hydrogen cyanide and 4 g/kg toluene. However, methods of analysis for the formulation are not required for these compounds because they can not be formed on storage. Methods can be required at Member State level. Also the usual requirement for spectra can be waived as these are well characterised compounds. Currently no FAO specification exists.

The content of sulcotrione in the representative formulation is 300 g/L (pure).

Beside the specification, 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 sulcotrione or the respective formulation.

The main data regarding the identity of sulcotrione and its physical and chemical properties are given in appendix 1.

However, sufficient test methods and data relating to physical, chemical and technical properties and analytical methods are available to ensure that at least limited quality control measurements of the plant protection product are possible. The outstanding issue is that at EU level methods for impurities that are not formed on storage are not a requirement. Without these methods the relevant impurities can not be monitored in the formulation.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. sulcotrione in food of plant origin and sulcotrione in soil and water. Although it is noted that the residue definition for soil and water is not finalised. The original air method in the DAR is no longer acceptable as it is not sensitive enough. The meeting of experts mammalian toxicology PRAPeR 44 significantly lowered the AOEL and this is why a new air method is identified as a data gap.

A multi-residue method like the Dutch MM1 or the German S19 is not applicable due to the nature of the residues.
The method of analysis for products of plant origin was by LC-MS/MS with an LOQ of 0.05 mg/kg. A method of analysis for products of animal origin is not required as MRLs will not be set see section 3.2. Soil can be analysed by LC-MS/MS with an LOQ of 0.01 mg/kg there is also an alternative HPLC-UV method with the same LOQ. Water can be analysed with a LC-MS/MS method with an LOQ of 0.1 µg/kg.

A method for body fluids and tissues is not required because sulcotrione is considered to be neither toxic nor very toxic.

2. Mammalian toxicology

Sulcotrione was discussed at the PRAPeR Expert's Meeting on mammalian toxicology (PRAPeR 44) in April 2008.

Although no technical specification had been agreed by the meeting on physical and chemical properties (PRAPeR 41), the meeting on toxicology considered that the batches used in the toxicological studies covered the technical specification as proposed by the applicant in the addendum 2 to volume 4 dated March 18, 2008.
The meeting agreed also that hydrogen cyanide, HCN, is a relevant impurity, however, at the given concentration in the technical specification, no toxicological concern is raised.
EFSA note: the relevance of toluene was not discussed at the meeting of experts, however in line with the decisions taken for other active substances, toluene would be considered as a relevant impurity for which no concern is raised at the level indicated in the technical specification.

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

In the rat and monkey, sulcotrione was rapidly absorbed and excreted, primarily in the urine, at an average of 93 % of the administered dose in the rat and 50-81 % in the monkey 96 hours after treatment. Excretion via faeces occurred in small amounts (2-6 %) in both species. Comparing faecal excretion data after intravenous application in rats and measurements of sulcotrione in the bile of monkeys, it was concluded that absorption from the gastrointestinal tract was complete upon oral administration.
Distribution of sulcotrione into tissues and organs was poor, there was no evidence of accumulation of residues, not even in the eye tissues that was identified as a target organ for toxicity; 96 hours after oral administration (rat), the majority of the remaining radioactivity was found in the liver and kidneys. Metabolism studies in rat and monkey showed that sulcotrione is poorly metabolised and over 91 % of the urinary radioactivity corresponded to unchanged parent. Small amounts of the parent molecule were metabolised by hydroxylation of the cyclohexanedione ring, forming either M02[3] (1-6 %) or M04[4] (< 1 %). The metabolite M01[5] (CMBA) which is formed by hydrolytic cleavage of the benzoyl moiety was detected in small amounts in urine (< 1 %); in the eye however, a different pattern of metabolism was revealed in the rat with 31 % of the radioactivity detected being CMBA. In contrast, monkey's metabolism pattern in ocular tissues did not differ substantially from the one in other tissues and 11 % of the radioactivity was identified as M02.

[3] M02 : 4-hydroxy-sulcotrione, 2-[2-chloro-4-(methylsulfonyl)benzoyl]-4-hydroxycyclohexane-1,3-dione
[4] M04 : 5-hydroxy-sulcotrione, 2-[2-chloro-4-(methylsulfonyl)benzoyl]-5-hydroxycyclohexane-1,3-dione
[5] M01 : 2-chloro-4-(methylsulfonyl)-benzoic acid (CMBA)

2.2. ACUTE TOXICITY

Sulcotrione presented low acute toxicity, either by the oral, dermal or inhalation route; no skin or eye irritation was observed. According to a Magnusson and Kligman test, 80 % sensitisation rate was obtained with sulcotrione at a 30 % dilution in corn oil, therefore classification with risk phrase R43 **"May cause sensitisation by skin contact"** was proposed.

2.3. SHORT TERM TOXICITY

Oral short term toxicity of sulcotrione was investigated in rats and dogs. Some studies were not considered acceptable (4-week rat, 16-week dog) mainly due to insufficient reporting as these were dose range-finding studies; deficient procedures were also reported in a 5-week rat study followed by a recovery phase, but 90-day studies in each the rat and dog, and a 1-year dog (capsule treatment) were considered as acceptable by the rapporteur Member State. A subchronic mechanistic study in rat was carried out on the causal relationship between increased levels of tyrosine and effects on liver and kidneys. Additional studies were performed on monkeys and rabbits to determine whether the corneal effects observed in rats and partly in dogs would also occur in these species; these studies were considered as supplementary information. A 4-week dermal study in rat was also provided.

The primary effects of sulcotrione, as characteristic 4-hydroxyphenylpyruvate dioxygenase (HPPD) inhibitor – a key enzyme of the tyrosine catabolic pathway, resulting in increased 4-hydroxyphenyl pyruvate, the proximal tyrosine metabolite and increased blood tyrosine concentration – were increased incidence of corneal lesions and increased liver and kidney weights, generally more prominent in males. The corneal lesions seen with the administration of HPPD inhibitors in rats have been accepted as a result of increased blood tyrosine or tyrosine metabolite concentration and were not considered relevant for humans during the evaluation of mesotrione[6] (a moderately strong HPPD inhibitor structurally very similar to sulcotrione). The effects observed in the liver and kidneys (increased organ weight, hepatocellular hypertrophy) and their relation with increased tyrosine concentration were discussed by the experts and, as a direct effect of sulcotrione on these organs could not be ruled out, they were considered relevant for human risk assessment. It was noted that, no eye lesions developed upon oral administration of sulcotrione up to 750 mg/kg bw/day in monkeys for one year and in rabbits after a three months treatment.

The NOAEL in rat was the dose level of **3.3 mg/kg bw/day** and the overall NOAEL in dog was 50 mg/kg bw/day. When applied dermally to rats, sulcotrione produced increased levels of blood tyrosine concentration from the low dose level of 50 mg/kg bw/day and up, but the NOAEL was considered to be the limit dose of 1000 mg/kg bw/day.

2.4. GENOTOXICITY

Inconsistent results were obtained from the package of genotoxicity studies conducted with sulcotrione. Some positive *in vitro* tests results consisted of two out of four Ames tests, a positive

[6] Scientific Committee on plants – SCP/MESOTRI/002-Final: Opinion on the Evaluation of mesotrione in the context of Council Directive 91/414/EEC concerning the placing of plant protection products on the market (Opinion adopted on July, 18 2002)

mouse lymphoma assay and a positive Sister Chromatid Exchange assay, although the latter was of doubtful relevance. In addition, one out of three *in vivo* micronucleus tests was also positive while the *in vivo* UDS test was negative. The experts considered that no evidence of carcinogenicity had been found in the long term studies and that higher relevance should be attributed to the results of the UDS assay due to toxicokinetic properties (distribution) of sulcotrione. Based on the weight of evidence, it was agreed that sulcotrione had no genotoxic potential *in vivo*.

2.5. LONG TERM TOXICITY

Long term toxicity was examined in a two-year study in rat and an 18-month study in mouse. A supplementary study was conducted to determine whether the corneal opacities and keratitis observed in the rat long term study were due to housing conditions or to sulcotrione administration.

The same kind of effects was observed in long term and short term studies related to HPPD inhibition. In the first rat study, from the lowest dose level of 2 mg/kg bw/day on, increased incidence of corneal opacities and keratitis were observed in both sexes, as well as liver and kidney effects; the NOAEL was below 2 mg/kg bw/day based on increased liver weight and, liver and kidney histopathology. In the supplementary rat study, the lower dose level of 0.04 mg/kg bw/day resulted also in increased incidence of kidney findings in males (enlargement, cystic changes and pelvis dilation) while ocular findings – that could be used as surrogate to demonstrate tyrosinaemia-related toxicity once tyrosine plasma levels were not determined in this study – were evident only from the next higher dose level of 0.4 mg/kg bw/day and above in males. The meeting agreed to set an **overall LOAEL for long term rat studies at 0.04 mg/kg bw/day**.

In the mouse, no corneal opacities were observed at any dose; the NOAEL was the dose level of 5.2 mg/kg bw/day based on increased liver weight at the next higher dose of 46 mg/kg bw/day; the higher dose (409 mg/kg bw/day) exceeded the maximum tolerated dose in females due to decreased survival. No evidence of treatment-related oncogenicity was found in either rats or mice.

2.6. REPRODUCTIVE TOXICITY

Reproductive toxicity of sulcotrione was tested in two 2-generation reproduction toxicity studies in rat and a developmental toxicity study in rat and in rabbit.

Reproduction toxicity

As in other rat studies, the adults (mainly the males) in the 2-generation studies showed effects on cornea, kidney (increased weight, protein filtrate, tubular basophilia, pelvis dilation) and liver (hepatocellular vacuolation). The **overall NOAEL for parental toxicity was the dose level of 0.06 mg/kg bw/day** based on increased liver and kidney weights, renal pelvis dilation and nephropathy observed at 0.6 mg/kg bw/day. No adverse effect on reproductive parameters was observed, therefore the NOAEL for reproductive effects was the highest dose tested of 340 mg/kg bw/day. Based on increased mortality, decreased body weight gain, delay in eye opening and urinary tract abnormalities apparent at 13.5 mg/kg bw/day, the offspring's NOAEL was set at 0.6 mg/kg bw/day; considering the relevance of the kidney findings observed in F_1 (first filial generation) and F_2 (second filial generation) generations but not in P_0 (parental) animals, the experts proposed a classification for sulcotrione with **Xn**, risk phrase **R63 "possible risk of harm to the unborn child"**.

Developmental toxicity

No developmental adverse effect was found in either rats or rabbits in the developmental toxicity studies. No corneal opacity was observed. Maternal toxicity in rats was limited to decreased body weight and food consumption, and increased liver weight at the highest dose of 1000 mg/kg bw/day; in the foetuses, the high dose produced a slight decrease in foetal weight and a slight increase in incomplete sternal ossification. Both maternal and foetal NOAELs were the dose level of 100 mg/kg bw/day.

In rabbits, decreased maternal food consumption and maternal body weight loss were observed during early pregnancy at 300 mg/kg bw/day; the maternal NOAEL was the dose of 100 mg/kg bw/day. No adverse effect was observed in the foetuses and the NOAEL for developmental toxicity was the highest dose tested of 300 mg/kg bw/day.

2.7. NEUROTOXICITY

In the 90-day dog study, neurological signs of toxicity were seen in parallel with systemic toxicity at 300 and 800 mg/kg bw/day, but these signs were not reproducible in the 1-year dog study. The experts agreed that no concern for specific neurotoxic potential was raised and therefore, no further neurotoxicity study was required.

2.8. FURTHER STUDIES

Metabolite CMBA

The metabolite CMBA was found to be a significant plant and soil metabolite but occurred in animal metabolism studies only at small concentrations. CMBA concentrates into the rat's eye since the eye metabolism is more pronounced than the one observed in other organs, so that about 30 % of sulcotrione that was distributed to the eyes was metabolised to CMBA. Toxicity studies on CMBA consisted of a full set of acute toxicity studies by the oral, dermal and inhalation route, eye and skin irritation and skin sensitization; repeated dose toxicity was investigated in 28-day and 90-day oral studies, 28-day inhalation study, and a 1-generation reproduction study. *In vitro* genotoxicity was examined in two Ames tests, a mouse lymphoma and a cytogenetic assay in human lymphocytes.

CMBA presented low acute toxicity and weak sensitization potential (5 %), not requiring classification, however it was severely irritant for the eyes and a classification as Xi, risk phrase R41 "risk of serious damage to eyes" is proposed.

In the short term studies, CMBA presented no adverse effect up to 1000 mg/kg bw/day in the 28-day study, but the experts agreed with the rapporteur Member State to lower the NOAEL of the 90-day study to 188 mg/kg bw/day based on slight increased incidence of epithelial cysts observed in the thymus at the highest dose of 763 mg/kg bw/day. The inhalation NOAEL was 1.20 µg/L air based on reversible squamous metaplasia of the ventromedial epithelium of the larynx at 11.84 µg/L air.

No adverse effects were observed on reproduction and offspring's parameters in the 1-generation study; the parental NOAEL was 267 mg/kg bw/day, based on slightly decreased body weight and food consumption and the NOAEL for reproductive and offspring's toxicity was 1035.4 mg/kg bw/day, the highest dose tested.

CMBA was negative in the four *in vitro* genotoxicity studies.

The experts noted that CMBA may have contributed to the whole pattern of eye effects, since keratitis is not usually related to tyrosinaemia, but was consistently observed in the rat's studies conducted with sulcotrione, concomitantly with the corneal lesions derived from the tyrosinaemia, however the metabolite itself did not cause tyrosinaemia up to the limit dose of 1000 mg/kg bw/day. No long term or developmental toxicity studies were available for CMBA. The most relevant NOAELs for CMBA were obtained from the 90-day oral, and the 1-generation rat studies; the experts agreed to set an overall NOAEL of 200 mg/kg bw/day for CMBA. Based on this overall NOAEL and applying a safety factor of 1000, due to the limited database available, the **ADI for CMBA was set at 0.2 mg/kg bw/day**.

Furthermore, the experts concluded that, according to the Guidance document on the assessment of the relevance of metabolites in groundwater[7], CMBA is of no toxicological relevance for groundwater, even if it exceeds the threshold value of 0.1 µg/L.

2.9. MEDICAL DATA

Routine medical examinations of plant personnel involved in sulcotrione production did not indicate any specific adverse effect on the health of employees, nor were there any sulcotrione related occupational incidents reported, in agricultural users or persons of the general population.

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

ADI

Initially in the draft assessment report, the rapporteur Member State proposed an ADI of 0.007 mg/kg bw/day based on the rat multigeneration study presenting a NOAEL of 0.7 mg/kg bw/day and a safety factor of 100; however the experts at the meeting lowered the multigeneration NOAEL to 0.06 mg/kg bw/day and the NOAEL from the 2-year rat study was changed to a LOAEL of 0.04 mg/kg bw/day.

The **ADI for sulcotrione was established at 0.0004 mg/kg bw/day** based on the LOAEL from the long term study in rat and an assessment factor of 100. The standard safety factor was considered sufficient based on the steep dose-response curve reaching rapidly a plateau.

AOEL

The rapporteur Member State proposed in the draft assessment report an AOEL of 0.007 mg/kg bw/day on the same basis as the ADI proposal. No further correction factor was necessary as oral absorption was shown to be complete.

The approach was agreed by the meeting considering the new NOAEL set for the multigeneration rat study of 0.06 mg/kg bw/day and a safety factor of 100. **The AOEL was set at 0.0006 mg/kg bw/day.**

[7] Guidance document on the assessment of the relevance of metabolites in groundwater of substances regulated under Council Directive 91/414/EEC: Sanco/221/2000-rev.10, of February 2003

ARfD

The rapporteur Member State proposed not to set an ARfD considering that the toxicological studies revealed no effect of concern with respect to an acute intake of sulcotrione. As the proposed classification with Xn, R63 was derived from the multigeneration studies where the effects were apparent through a continuous dietary administration, it was not considered relevant for the setting of an ARfD. The experts agreed with this approach and **no ARfD was allocated.**

2.11. DERMAL ABSORPTION

Dermal absorption was investigated *in vitro* with the representative formulation, Mikado, and a 1/133 (v/v) spray dilution of the formulation through human epidermis. Based on this study, dermal absorption was considered 0.1 % for the concentrate and 0.5 % for the in-use field spray dilution.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Mikado is a suspension concentrate (SC) formulation containing 300 g sulcotrione/L. It is a post-emergence herbicide which is used for the control of broadleaf weeds and some grasses in maize. Applications of Mikado will be achieved via field crop sprayers at a maximum dose rate of 0.450 kg sulcotrione/ha, corresponding to 1.5 L product/ha, and a spray volume of 200-400 L/ha.

Estimation of operator, worker and bystander exposure were recalculated in the addendum 3 to volume 3 of May 2008 based on the parameters agreed at the PRAPeR expert meeting.

Operator exposure

The operator exposure estimates were calculated using both the German and the UK POEM models. According to the German model assumptions, the body weight of operators is 70 kg and 20 ha are treated per day. According to the UK POEM, body weight of operators is 60 kg and 50 ha are treated per day, packaging of 5 L (wide neck) was considered.

Estimated operator exposure presented as % of AOEL (0.0006 mg/kg bw/day) in maize, application rate of 0.450 kg sulcotrione/ha

Tractor-mounted (field crop)	No PPE	With PPE[(a)] during M/L	With PPE[(b)] during M/L & application
UK POEM	1797	1683	583
German model	304	253	50.2

[(a)] PPE: gloves during mixing and loading (M/L)

[(b)] PPE: gloves (M/L & application), protective garment and sturdy footwear (application)

According to the UK POEM, estimated exposure of operators is above the AOEL even considering the use of PPE; according to the German model, the estimated exposure of operators is below the AOEL only if PPE, as gloves during mixing/loading and application, and coverall and sturdy footwear during application are worn.

Worker exposure

Estimation of worker exposure was performed according to the model developed by the German BBA (Hoernicke E. *et al.* 1998). Transfer factor of 1500 [cm^2/person/h] was considered appropriate during the meeting of experts; default value of 60 kg for worker body weight, dermal absorption of 0.5 % and penetration through clothing (PPE) of 5 % were used in the calculations.

Estimated worker exposure presented as % of AOEL (0.0006 mg/kg bw/day)

Worker exposure	No PPE	With PPE [(a)]
Scouting activities/monitoring the crop	75.0	3.8

[(a)] PPE: protective gloves

Therefore, after the spray solution has dried, the estimated exposure to sulcotrione during re-entry operations does not exceed the AOEL, even if no PPE are worn.

Bystander exposure

Estimation of bystander exposure considered both dermal exposure derived from available drift data (Ganzelmeier *et al.* 2000), and inhalation exposure derived from the German model operator exposure. The drift rate during spraying in field crops at a distance of 7 m from the spray equipment was 0.41 %; a default surface area of 2 m^2/person was assumed. Using the proposed absorption rates of 0.5 % for dermal exposure (diluted spray) and 100 % for inhalation exposure, the estimated bystander exposure represents **5.45 % of the AOEL** of 0.0006 mg/kg bw/day.

3. Residues

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

The metabolism of sulcotrione has been investigated in maize after post emergence application, reflecting the representative use supported by the applicant. The metabolic degradation of sulcotrione is essentially focused to the cyclohexanedione ring and the CMBA metabolite appears to be the end product of the plant metabolism. This compound is the major constituent of the residue pattern in maize forage and grains, representing 29 and 53 % of the Total Radioactive Residues (TRR) in these matrices, respectively. Uptake of this compound by the roots, as a result of soil metabolism of sulcotrione, is supposed to contribute to its predominance in the metabolic pattern. Beside CMBA, sulcotrione is also present in trace amounts (less than 1 % of the TRR) in grains and forage, as well as hydroxylated derivatives (less than 5 % of the TRR). It is also postulated from experiments with excised leaves that fragments resulting from the degradation of the cyclohexanedione ring consist in aliphatic carboxylic acids such as glutaric and succinic acids.

The residue definition for risk assessment and monitoring was proposed in the DAR to consist of sulcotrione only. The meeting of experts PRAPeR 45 considered that CMBA is the main metabolite in the maize metabolism study and is present in the feed items at much higher levels than the parent

compound. According to the toxicological section the metabolite is less toxic than the parent compound. Also the residue trials on maize indicate significant residue levels in the feed items. By consequence the need for a livestock metabolism study is triggered for metabolite CMBA and although the RMS is not in favour the meeting decided to include CMBA in the residue definition for risk assessment. The residue definition for monitoring remains as sulcotrione.

Finally, the meeting of experts noted that according to the available livestock metabolism study residues of CMBA in the animal commodities are anyway not expected. So there is no need to set MRLs for products of animal origin.

A sufficient number of supervised residue trials have been conducted in Northern and Southern European regions. Residues of sulcotrione and CMBA in mature maize grains or sweet corn were consistently below the Limit Of Quantification (LOQ). In maize plant at forage stage, residues of sulcotrione were not detected, but residues of CMBA were present up to 0.2 mg/kg. The reliability of these results is supported by storage stability studies demonstrating that residues of sulcotrione and CMBA are stable under deep freeze conditions for 2 years.
Considering that no residues are present in raw plant products to be processed, processing studies were not considered necessary.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Considering the short soil DT50 and DT90 values of sulcotrione and CMBA, rotational crops studies were not considered necessary. No plant back restriction related to the uptake of residues by rotational crops is necessary.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

As indicated from supervised residue trials livestock are not exposed to significant levels of sulcotrione through consumption of maize grain or forage. As the physico-chemical properties do not suggest any accumulation potential, livestock metabolism studies conducted with sulcotrione are not necessary.
Due to the fact that the major metabolite CMBA may occur in maize forage in significant amounts, a metabolism study in lactating goats was conducted with this metabolite. This study was conducted with an exposure rate of the animals 10 times higher than the expected critical exposure of ruminants in practical conditions. Under these conditions the TRR were below 0.005 mg/kg in milk and all edible tissues, with the exception on kidneys showing TRR of 0.04 mg/kg. The nature of residues was determined in kidneys only and consisted essentially (80 % of the TRR) of CMBA.
Considering these results, quantifiable levels of CMBA are not expected in animal commodities.
A residue definition and MRLs in animal products, related to the representative use of sulcotrione in maize are not necessary.

3.3. CONSUMER RISK ASSESSMENT

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 as well as the EFSA model. Residues in maize grains were considered to be at the level of proposed MRL (LOQ). Based on these assumptions, the calculated TMDIs were below 31 % of the ADI for both considered populations of consumers.

As CMBA is a significant but non relevant metabolite in ground water at a level above 0.75 µg/L a consumer risk assessment is required. The risk assessment for CMBA gives a highest intake of <0.2 % of the ADI for CMBA.

A short term dietary risk assessment was not conducted as no ARfD is considered necessary.

3.4. PROPOSED MRL

Considering the results of supervised residue trials it is proposed to set the MRL for sulcotrione residues at 0.05* mg/kg (* indicates that the MRL is set at the level of the limit of quantification of the method of analysis). A MRL for products of animal origin is not necessary.

4. Environmental fate and behaviour

Sulcotrione was discussed at the PRAPeR experts' meeting on fate and behaviour in the environment (PRAPeR 42) in March/April 2008 on basis of the Addendum 1 (March 2008) to the DAR.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

The aerobic route of degradation of [phenyl-UL-^{14}C]sulcotrione was studied in 3 soils (silt loam, sand and sandy loam) with application rates of 1 and 100 ppm and at temperatures of 5 ºC (for 1 ppm only) and 25 ºC. Mineralisation of sulcotrione was found to be extensive with >50% AR (applied radioactivity) after 120 days in the silt loam and sand soils at 1 ppm and 25 ºC. Mineralisation was insignificant (< 3% AR) in the sandy loam. The mineralisation was also insignificant in the silt loam soil incubated at 5 ºC or treated with the exaggerated rate of 100 ppm. Unextracted radioactivity at day 120 ranged between 5.9 and 26.5% AR in all the tests.

Only one major metabolite, **CMBA**, was detected in the extracts of all three soils (max 60.3% AR at 120d).

In the sterile controls degradation of sulcotrione and formation of metabolites (i.e. CMBA) was of minor importance.

Based on the available information it was proposed that the degradation of sulcotrione proceeds through the cleavage of the cyclohexane moiety and the formation of CMBA which is further mineralised. In the original DAR it was asserted that further investigation with other radiolabels (i.e. in the cyclohexanedione ring) was not necessary as the degradation of the cyclohexanedione moiety would results in the formation of naturally occurring compounds, e.g. succinic and glutaric acid. However, the experts from the member states agreed that the formation of the intermediate

degradation product 1,3-cyclohexanedione (a metabolite potentially formed in aquatic systems, see section 4.2.1) can not be excluded. Therefore, a data gap was identified in the PRAPeR meeting 42 for an aerobic soil degradation study with sulcotrione labelled in the cyclohexanedione ring or for evidences to demonstrate that potential metabolites containing the cyclohexanedione ring are labile.

Under anaerobic conditions sulcotrione and its major residues in soil are practically stable. Sunlight is not regarded as a relevant environmental process for degrading sulcotrione on soil surface. However, it was indicated that the influence of sunlight enhances the degradation of sulcotrione to CMBA.

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

The rate of degradation of sulcotrione in soil was estimated from the results of the studies conducted at 25 ºC with test concentration of 1 ppm as described in 4.1.1 above. Additionally, 2 soils were investigated in darkness (20 ºC and 40% MWHC soil moisture) with non-radiolabelled sulcotrione. Estimated DT_{50} (single first order non linear regression) were 14.1-74.0 days for sulcotrione (n=5) and 12.2-44.8 days for CMBA (n=4 as a statistically value could not be analysed based on the experimental data). After normalisation to FOCUS reference conditions[8] (20°C and -10kPa soil moisture content) these single first order DT_{50} were in the range 10.8-89.7 days (geometric mean = 25.3 days) for sulcotrione and 9.4-38.2 days (geometric mean = 24.2 days) for CMBA.

Soil dissipation studies were performed in 1990-1993 in Southern France (2 trials, soil cropped with maize), Italy (3 trials, soil cropped with maize) and Germany (4 trials, bare soil) up to a nominal application rate of 600 g a.s./ha. Suction lysimeters were installed at each trial site down to a depth of 90 cm. Further details on the kinetic evaluation of the field dissipation behaviour of sulcotrione and CMBA and the normalisation procedure for standardisation of field DT_{50} to FOCUS reference conditions were provided in Addendum 1. During the meeting of experts concerns arose over the method used to estimate the field DT_{50} values. The EFSA agrees with the explanation provided by RMS in Addendum 3 that the appropriate residues summation over all sampled soil layers was already considered in the kinetic re-evaluation of the field data presented in the DAR

The kinetic modelling analysis led to the first-order normalised DT_{50} values for sulcotrione and its metabolite CMBA in the range of 1.2-11.4 days and 2.5-45.4 days, respectively. The non-normalised DT_{50} values were recalculated with ModelMaker by the RMS for all the trials and presented in Addendum 3. As this evaluation was presented after the experts' meeting, these values are not peer reviewed.

The experts from the member states discussed if it might be possible to use the estimated normalised field DT_{50} values for FOCUS modelling. The concern was that in particular for leaching processes that may have occurred during the field dissipation trials. It was noted that in three out of the nine trials (Italy: Emilia Romagna, Lombardia and Veneto) residues of sulcotrione and CMBA were determined in soil at depths below 10 cm and/or in some soil-pore water samples down to a depth of

[8] Using section 2.4.2 of the generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.

90 cm. The experts agreed that it can not be excluded that in the Italian trials some fraction of the dose can have leached out of the soil layers that were sampled and therefore the related dissipation DT_{50} values for sulcotrione and CMBA can not be used as degradation rates in soil. Consequently, the appropriate geometric mean normalised DT_{50} values to be used in FOCUS modelling should be 3.6 days for sulcotrione and 8.5 days for CMBA.

Predicted environmental concentrations (PEC) in soil were recalculated based on the non-normalised maximum field DT_{50} (= 13.0 days with linear regression) for sulcotrione and maximum normalised laboratory DT_{50} for CMBA (Addendum 1). Following the request by the experts for new PECsoil calculations using the non linear regression no-normalised longest field DT_{50} for sulcotrione, the new evaluation was provided by RMS and reported in Addendum 3. Even if the use of the field DT_{50} of 16.5 days (from soil Veneto) is not recommended as it represents dissipation rate rather than degradation, the EFSA considers the estimates acceptable.

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

Sorption properties of sulcotrione in soil were investigated in batch equilibrium tests as well as column leaching experiments without soil ageing. The Freundlich adsorption constants $K_f oc$ determined in batch equilibrium tests performed with 5 different soils ranged from 17 to 58 mL/g (mean = 36 mL/g), Freundlich coefficients 1/n ranged from 0.812 to 0.888 (mean = 0.839). Regression analysis indicated that the adsorption of sulcotrione is not only determined by the organic carbon content of the soil but at least also by the pH value, which itself correlated to the organic carbon content. Taking into consideration the very high mobility of sulcotrione in soil, it was agreed that the potential soil pH dependence of adsorption of sulcotrione is not expected to have a significant effect in the results for groundwater modelling.

The results of a parent column leaching study performed with four soils indicated a similar K_d value (on average 0.81 mL/g) as that found by the batch equilibrium studies.

For the major soil metabolite CMBA Freundlich adsorption constants $K_f oc$ were determined in batch tests with five soils. Estimated $K_f oc$ varied from 1.08 to 8.98 mL/g (mean = 4.76 mL/g), Freundlich coefficients 1/n ranged from 0.708 to 0.931 (mean = 0.861). Metabolite CMBA can be classified as very high mobile in soil. There was no evidence of a correlation of adsorption with soil pH.

The meeting of experts concluded that the adsorption/desorption study (Muller et al., 1994) that was rejected by the RMS, can be considered acceptable. Since the exclusion of the results from this study makes the assessment a worst case, it was agreed that member states may re/assess it for their nation registrations if necessary.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Sulcotrione is stable to hydrolysis in buffer solutions of pH 5,7 and 9 at 25ºC.

Photolysis in buffered solution at pH 7 takes place to a certain, but not high extent, even if the quantum yield calculated from absorption spectra and degradation rates measured in pure water indicates that photolysis could be a reasonable route for dissipation of sulcotrione from the aqueous

environment. The only transformation product found in the available abiotic studies was CMBA (max. 27% AR). The experts confirmed the validity of the available aqueous photolysis study and agreed there was insufficient satisfactory information to confirm that the photo degradation product 1-H-xanthene-1,9-dione-3,4-dihydro-6-methylsulfonyl is formed in significant amounts as reported in open literature[9].

Biological degradation of ^{14}C-phenyl -sulcotrione was studied in two different water-sediment systems. The need for a corresponding study to be carried out using ^{14}C-cyclohexanedione-sulcotrione was discussed at the meeting of experts. The peer review had questions over the metabolite 1,3-cyclohexanedione, which some recent open literature[10] indicated to be an hydrolysis product together with CMBA. It was noted that the hydrolysis study provided by the applicant was conducted with sulcotrione radiolabelled in both the phenyl and cyclohexanedione ring, but in the dark water-sediment study only the phenyl radiolabelled position was investigated. On balance, the experts agreed that 1,3-cyclohexanedione was probably not formed under sterile hydrolysis conditions but it cannot be excluded that it would not be formed in significant amounts under natural conditions in biological sediment waters systems. Therefore, a data gap was identified by the experts for a water-sediment study with ^{14}C-cyclohexanedione sulcotrione or for evidences that the cyclohexanedione ring is labile in aquatic systems.

In the available water-sediment study (20ºC in the dark, a loamy sand sediment with 2.1% OC and a silt loam sediment with 15.1% OC) sulcotrione partitioned to the sediment with radioactive levels in the water phase declining to *ca* 30% AR after 30 days. After this point, a decrease in the radioactivity recovered from the sediment was also observed with radioactive residues declining from a maximum of 47.2-49.8% AR to 17.0-27.3% AR at the study end. Degradation resulted in the formation of the major metabolite CMBA, the levels of which increased steadily throughout the study (max 42.2% AR in the surface water and max 18.6% AR in the sediment after 100 days). First order DT_{50} values of sulcotrione were calculated to be 6 and 15 days in the surface water and 48 and 84 days in the total aquatic system (water and sediment). No reliable DT_{50} values for the metabolite CMBA are available.

Aquatic exposure concentrations of sulcotrione have been calculated as higher tier at FOCUS Step 3 level. PECsw (Predicted Environmental concentration in surface water) were calculated for the metabolite CMBA at Step 2 level to demonstrate a safe use under European conditions. As worst-case application scenario, one foliar ground spray application of 450 g/ha sulcotrione to maize was considered. Originally simulations were carried out with the geometric mean of the FOCUS normalised soil $DT_{50field}$, which is 4.3 days for sulcotrione and 13.9 days for CMBA. A geometric mean DT_{50} in the total system of 64 days was used for both compartments for sulcotrione and a default value of 999 days for CMBA. The experts agreed that these DT_{50} values represent worst cases and therefore the calculations are considered acceptable.

[9] Environ. Sci. Technol. **2006**, *40*, 2989-2995.
[10] J. Agric. Food Chem. **2005**, *53*, 4091-4095.

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

Predicted environmental concentrations of sulcotrione and its major metabolite CMBA in groundwater were estimated using the simulation model FOCUS-PEARL. The results showed that for sulcotrione no concentration in the percolate at 1 m soil depth exceeding 0.001 µg/L is to be expected. CMBA concentrations (80th percentile annual average concentration at 1 m) are in the range of 0.015 – 1.462 µg/L. The concentration of 0.1 µg/L is exceeded in 6 out o 8 European FOCUS scenarios parameterised for maize, and for Hamburg and Okehampton scenarios the estimated PEC_{gw} are > 0.75 µg/L. These findings trigger, according to the *Guidance document on the assessment of the relevance of metabolites in groundwater of the substances regulated under Council Directive 91/414/EEC*"(SANCO 221/2000, final 2003) a 3-stage hazard assessment comprising a biological, genotoxicity and toxicity screening. The toxicological assessment was able to conclude that CMBA is not relevant regarding groundwater at the expected concentrations (see section 2.8).

4.3. FATE AND BEHAVIOUR IN AIR

The vapour pressure of sulcotrione was determined to be 5.3×10^{-6} Pa at 25 C. On the basis of this value and the Henry's Law constant it can be concluded that due to the low vapour pressure no significant evaporation of sulcotrione has to be expected after its use. Thus was confirmed by experiments spraying SC formulated sulcotrione on soil and leaf surface.

The half-life of sulcotrione in the troposphere was re-calculated by the RMS in Addendum 1. Assuming a 12-hour-day with an OH radical concentration of 1.5 x 10^6 OH/cm^3 the DT_{50} of sulcotrione in air amounts to 1.424 days.. According to these results an accumulation of sulcotrione in the air and a contamination by wet or dry deposition are not to be expected.

5. Ecotoxicology

Sulcotrione was discussed at the PRAPeR experts' meeting for ecotoxicology (PRAPeR 43) in April 2008.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The representative use evaluated is the use as an herbicide in maize (1 x 0.45 kg sulcotrione/ha). The acute and short-term toxicity of sulcotrione to birds is low with LD_{50} values of >1350 mg/kg bw and >1259 mg/kg bw/d. Two long-term (reproduction) studies with mallard duck (*Anas platyrhynchos*) were submitted. The RMS suggested using the NOEC of 17 mg/kg bw/d from the 6-week reproduction study. The experts agreed to use the NOEC from the 6-week reproduction study. The lower NOEC of 10.9 mg a.s./kg bw/d observed in the 20 week reproduction study was considered as less robust since the effects did not follow a dose response relationship.

The acute and short-term TERs in the first tier risk assessment were above the Annex VI trigger of 10. The first-tier long-term TERs were below the trigger of 5 indicating a potential high long-term

risk. The refined risk assessment for medium herbivorous birds resulted in TERs >5 based on residue decline. *Motacilla alba* (white wagtail), *Alauda arvensis* (skylark) and *Vanellus vanellus* (lapwing) were chosen as focal species to refine the long-term risk assessment for insectivorous birds. The experts rejected the suggested PT refinements since they were not sufficiently supported by data (no radio-tracking). The PD refinements were agreed by the experts (white wagtail: 100% large insects after early application and 50% large and 50% small insects for applications late after emergence, skylark: 60% large insects and 40% small insects, lapwing: 100% large insects). Only the TER for lapwing exceeds the trigger of 5 based on the agreed refinements of PD. A data gap was identified in the expert meeting for the applicant to provide a new refined risk assessment for insectivorous birds. A new study (Wolf C., 2005) was submitted by the applicant which provides information on the potential focal species in maize and sugar beet fields including radio-tracking data to investigate the time spent foraging in the field. According to commission regulation 1095/2007 this information can not be taken into account in the peer-review. The study and a refined risk assessment based on this study were included by the RMS in the not peer-reviewed addendum 3 from May 2008.

The toxicity of the major plant metabolite CMBA was low in a short-term dietary study with mallard duck (LD50 >2010 mg CMBA/kg bw/d). The short-term TER was calculated as >147 for herbivorous birds assuming that the amount of CMBA equals the parent sulcotrione.

The acute and toxicity of sulcotrione to mammals is low (LD_{50} values >5000 mg/kg bw). The acute TER for a medium herbivorous mammal is >456 indicating a low risk. The first-tier long-term TER of 0.015 is significantly below the trigger of 5. The refined risk assessment is based on residue decline and a refinement of the PT value (0.26) for hare (*Lepus europaeus*). The suggested refinement of the PT value of 0.26 for hare was not sufficiently supported by data and hence not accepted by the experts. The long-term endpoint (NOEL of 0.04 mg sulcotrione/kg bw/d) was based on ocular effects. In other studies no effects were observed at higher dose rates (0.4 to 0.5 mg a.s./kg bw/d). Ocular effects were observed only after long dietary exposure in the tests while sulcotrione dissipates rapidly. The experts agreed that effects observed in the reproduction study are of higher relevance and suggested to use the reproductive endpoint (NOEL of 0.5 mg a.s./kg bw/d) in the long-term risk assessment. A new study (Wolf C., 2005) was submitted to refine the PT values. The study was included in the not peer-reviewed addenda. Based on the refinements agreed in the expert meeting and the new long-term endpoint the long-term the TER for medium herbivorous mammals was above the trigger of 5 indicating a low risk.

The acute and chronic toxicity of the plant metabolite CMBA to mammals is low (acute LC_{50} >2000 mg/kg bw, long-term NOEC = 969 mg/kg bw/d). The first-tier TERs were calculated as >182 and 363 based on the assumption that the amount of CMBA equals the parent sulcotrione.

The risk from uptake of contaminated drinking water was assessed as low for birds and mammals.

Overall it is concluded that the risk to mammals is low for the representative use of sulcotrione. The acute and short-term risk to birds was assessed as low but a potential high long-term risk to birds cannot be excluded on the basis of the peer-reviewed information.

5.2. RISK TO AQUATIC ORGANISMS

Sulcotrione is of low acute toxicity to fish and aquatic invertebrates. The lowest endpoint was observed for aquatic plants. The E_bC_{50} of 0.051 mg sulcotrione/L observed in the study with *Lemna gibba* drives the aquatic risk assessment. The toxicity of sulcotrione is not significantly increased when formulated as MIKADO SC300. The TERs for all groups of aquatic organisms were greater than the Annex VI triggers of 100 and 10 except for *Lemna gibba*. Only one (R4 stream) out of seven FOCUS step 3 scenarios resulted in a TER <10 indicating that the risk to aquatic organisms is low for most geoclimatic conditions in Europe. Risk mitigation measures are required under environmental conditions represented by scenario R4.

The metabolite CMBA is of low toxicity to aquatic organisms including *Lemna gibba*. The lowest endpoint was observed for algae E_bC_{50} of 34 mg CMBA/L. The Annex VI triggers were met with FOCUS step2 PECsw.

The potential of bioconcentration of sulcotrione and its metabolite CMBA is low since the log P_{ow} values are <3.

5.3. RISK TO BEES

Acute oral and contact toxicity studies were conducted with technical and formulated sulcotrione showing similar toxicity of the a.s. when formulated. In addition six acute oral studies with formulated sulcotrione were submitted. The HQ values were <50 indicating a low risk to bees for the representative use

5.4. RISK TO OTHER ARTHROPOD SPECIES

Standard laboratory tests were conducted with the formulation Mikado SC300 and the indicator species *Aphidius rhopalosiphi* and *Typhlodromus pyri*. The in-field and off-field HQ values were <2 for both species. Additional species were tested and no effects of >50% were observed in standard laboratory tests with *Poecilus cupreus* and *Aleochara bilineata*. However effects on mortality/reproduction of >50% were observed in tests with *Coccinella septempunctata* and *Pardosa sp* at the suggested application rate of 450 g sulcotrione/ha. Fresh residues on maize leaves resulted in 31.9% mortality and fertility of *C. septempunctata* was increased by 83.5%. After 7 days of ageing only 3.3% mortality was observed. Reproduction was still significantly increased by 79.7%. The mortality observed in the extended laboratory studies was <50% and hence the trigger for in-field effects was met. The increase in reproduction is not considered as an adverse effect. The off-field risk for *C. septempunctata* was assessed as low because <50% mortality was observed when exposed to fresh residues on maize plants.

Several extended laboratory studies were conducted with *Pardosa sp*. The mortality of lycosid spiders was 38.2% at 14 days and 88.2% at 21 days if exposed to fresh residues. The mortality was <50% after 14 days of ageing of residues. This meets the trigger to show the potential of recolonisation of the in-field area. However even after 42 days of ageing the residues still led to a statistically significantly increased mortality. No increased mortality was observed when the animals were exposed to residues after 56 days of ageing. A severe impact on lycosid spiders in the in-field area is expected and due to the long persistence of effects it is uncertain if recolonisation would occur in a real field situation. No further information was made available to demonstrate recovery/recolonisation of spiders in the in-field area. The LR_{50} for *Pardosa sp*. was calculated as 10.34 g a.s./ha which is below the calculated off-field exposure rate of 12.47 g a.s./ha indicating a potential high risk for spiders in the off-field area. It was agreed by the experts that risk mitigation measures should be applied to ensure that recolonisation of the in-field area is possible from unaffected off-field areas as proposed by the RMS. Risk mitigation comparable to an in-field no spray-buffer zone of 5m is recommended.

5.5. RISK TO EARTHWORMS

The acute toxicity to earthworms of technical and formulated sulcotrione and its major soil metabolite CMSBA are low with (14d) LC_{50} values of >1000 mg/kg soil. No chronic testing with sulcotrione was triggered since the DT_{90}(f) is <100 days and it is applied only once per year. A chronic study with the metabolite CMBA showed a low chronic toxicity to earthworms. No significant sublethal/reproductive effects were observed up to the highest tested concentration of 1000 mg CMBA/kg soil. The TERs were several orders of magnitude above the triggers of 10 and 5 indicating a low risk to earthworms.

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

No studies with sulcotrione are required since the field DT_{90} in soil is <100 d and the product is applied only once a year. A study with *Folsomia candida* and the major metabolite CMBA was submitted. The study was re-evaluated in addendum 1 from March 2008. The 28d LD_{50} of >1000 mg/kg soil and the NOEC for reproduction of 32 mg CMBA/kg soil were agreed by the experts. The resulting TERs are far above the trigger of 5 indicating a low risk to collembolans.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

No effects of >25 % on soil respiration and nitrification were observed in tests with formulated sulcotrione and its major soil metabolite CMBA up to concentrations of 4.5 mg sulcotrione/kg soil and 1 mg CMBA/kg soil. The maximum PECs were calculated as 0.45 mg sulcotrione/kg soil and 0.157 mg CMBA/kg soil. Therefore the risk to soil non-target micro-organisms is considered to be low for the representative use evaluated.

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

Herbicidal effects of formulated sulcotrione on vegetative vigour and emergence were investigated in several tests with mono- and dicotyledon plant species showing that dicotyledons are significantly more sensitive. The lowest ER_{50} values were observed for *Lactuca sativa*. The ER_{50} for seedling emergence was 7 g a.s./ha and for vegetative vigour 2 g a.s./ha. The TERs were above the trigger of 5 for seedling emergence if a no-spray buffer zone of 5m is applied and 50% interception is taken into account (without interception the TER is 2.7). For the vegetative vigour the TERs are below 5 even at a no-spray buffer zone of 5m. The risk was refined using the geometric mean of all available ER_{50} values for *Lactuca sativa* from the different tests. Based on the ER_{50} of 3.3 the TER is 5.1 if a 10 m no-spray buffer zone and 50% drift reduction nozzles are applied. As a further risk assessment approach the HC_5 was calculated as 2.58 based on the endpoints of 10 different species. An assessment factor of 2 was suggested to be used by the RMS to account for uncertainties concerning the extrapolation of the effects from the lab to the field conditions and effects on plant communities due to competition effects because of differences in sensitivity. Risk mitigation comparable to a no-spray buffer zone of 10 m is required based on the HC_5 and an assessment factor of 2. The experts agreed to the risk assessment presented by the RMS. Overall it is concluded that a high risk to non-target plants in the off-field area is indicated and risk mitigation measures comparable to an in-field no spray buffer zone of 10 m are required.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

Sulcotrione and CMBA were tested with activated sewage sludge. The EC_{50} for respiration was 4060 mg sulcotrione/l and 60 mg CMBA/L. Technical sulcotrione and its metabolite CMBA did not lead to adverse effects on *Pseudomonas putida* up to the highest tested concentrations of 180 and 100 mg/L. It is not expected that the concentrations of sulcotrione and CMBA in biological sewage treatment plants would reach concentrations high enough to cause adverse effects if the product is applied according to the GAP. Therefore the risk to biological methods of sewage treatment is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: sulcotrione, CMBA[11], data gap regarding potential metabolites containing the cyclohexanedione moiety (i.e. 1,3-cyclohexanedione)

Definitions for monitoring[12]: sulcotrione

[11] CMBA 2-chloro-4-(methylsulfonyl)-benzoic acid

[12] Definitions for monitoring provisional pending on the results of the required studies/information identified in the data gaps in the environmental fate section.

Water

Ground water

Definitions for exposure assessment: sulcotrione, CMBA, data gap regarding potential metabolites containing the cyclohexanedione moiety (i.e. 1,3-cyclohexanedione)

Definitions for monitoring[12]: sulcotrione

Surface water (water and sediment)

Definitions for risk assessment: sulcotrione, CMBA, data gap regarding potential metabolites containing the cyclohexanedione moiety (i.e. 1,3-cyclohexanedione)

Definitions for monitoring[12]: sulcotrione

Air

Definitions for risk assessment: sulcotrione

Definitions for monitoring: sulcotrione

Food of plant origin

Definitions for risk assessment: sulcotrione and CMBA expressed as sulcotrione

Definitions for monitoring: sulcotrione

Food of animal origin

Definitions for risk assessment: not necessary

Definitions for monitoring: not necessary

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
sulcotrione	Moderate to medium persistence Single first order DT_{50} 10.8-89.7 days (20°C, pF2 soil moisture)	Low toxicity and low risk to soil dwelling organisms.
CMBA	Low to moderate persistence Single first order DT_{50} 9.4-38.2 days (20°C, pF2 soil moisture)	Low toxicity and low risk to soil dwelling organisms.

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
sulcotrione	Very high mobility K_{foc} 17-58 mL/g	No	Yes	Yes	Yes
CMBA	Very high mobility K_{foc}	FOCUS PEARL 1.5.8: yes, trigger exceeded in 6 out of 8	No	Not relevant, however an ADI of 0.2 mg/kg bw/day	No

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
	1.1-9.0 mL/g	scenarios (max 1.462 µg/L for Hamburg scenario) ; trigger 0.75 µg/L exceeded for 2 scenarios		was established for the metabolite	

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
sulcotrione	Low toxicity to fish and aquatic invertebrates but very toxic to aquatic higher plants. The risk to aquatic plants was assessed as low except for the FOCUS step 3 scenario R4.
CMBA	Low toxicity and low risk to aquatic organisms.

Air

Compound (name and/or code)	Toxicology
sulcotrione	Inhalation rat LC_{50} > 1.63 mg/L air/4 h, highest technically available concentration, no classification proposed

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

- Maximum content of sulcotrione in the technical concentrate TK has been identified as a data gap (relevant for all uses, data gap identified by meeting of experts April 2008, date of submission unknown, refer to chapter 1)
- Further information on the impurity profile of the TK with regard to the possible loss of other volatile components when the TK was dried for analysis (relevant for all uses, data gap identified by meeting of experts April 2008, date of submission unknown, refer to chapter 1)
- Confirm how the identity of impurities 4 and 5 were established (relevant for all uses, data gap identified by meeting of experts April 2008, date of submission unknown, refer to chapter 1)
- Analytical method for the determination of sulcotrione in air with an LOQ of 0.18 µg/m³ (relevant for all uses, data gap identified by meeting of experts April 2008, date of submission unknown, refer to chapter 1)
- Aerobic soil degradation study performed with sulcotrione radiolabelled in the cyclohexanedione-ring or evidences to demonstrate that potential metabolites containing the cyclohexanedione ring are labile (relevant for all representative uses evaluated; data gap identified by meeting of experts PRAPeR 42; date of submission unknown,; refer to point 4.1)
- A water-sediment study performed with sulcotrione radiolabelled in the cyclohexanedione-ring or evidences to demonstrate that potential metabolites containing the cyclohexanedione ring are labile (relevant for all representative uses evaluated; data gap identified by meeting of experts PRAPeR 42; date of submission unknown,; refer to point 4.2)
- A refined risk assessment for insectivorous birds is needed (relevant for all uses evaluated; data gap identified in the experts' meeting PRAPeR 43 in April 2008; new data were submitted by the applicant but not peer-reviewed; refer to point 5.1)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as a herbicide on maize. Full details of the GAP can be found in the attached list of end points.

The representative formulated product for the evaluation was "Mikado", a suspension concentrate (SC).

Adequate methods are available to monitor all compounds given in the respective residue definition.

Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues. It is noted that the residue definitions for soil and water are not yet finalised.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that some quality control measurements of the plant protection product are possible. Data gaps have been identified for the specification, and for a new method of analysis for sulcotrione in air.

The acute toxicity of sulcotrione was low, it did not present eye or skin irritation properties; however, it was proposed to classify the active substance with risk phrase R43 "may cause sensitisation by skin contact" according to a Magnusson & Kligman test.

Sulcotrione is a 4-hydroxyphenylpyruvate dioxygenase (HPPD) inhibitor, a key enzyme of the tyrosine catabolic pathway, resulting in increased 4-hydroxyphenyl pyruvate, the proximal tyrosine metabolite and increased blood tyrosine concentration. Male rats were recognised as being more sensitive to sulcotrione, and primary effects in short term and long term studies were characterized by corneal lesions and increased liver and kidney weights associated with histopathological findings. Corneal lesions have been shown to be irrelevant for human risk assessment, but liver and mainly kidney effects were considered as sulcotrione-mediated effects and relevant for human risk assessment. Inconsistent results were obtained from genotoxicity studies, but it was concluded, based on the weight of evidence, that sulcotrione had no genotoxic potential *in vivo*. No potential for carcinogenicity was found either.

Reproduction toxicity studies reflected the same effects in parents, but abnormalities of the urinary tract were increased in pups of both generations, not observed in the first parental animals, and on this basis, a classification with Xn, R63 "possible risk of harm to the unborn child" was proposed; no effect on the reproduction or fertility was observed. No developmental effects were observed in either rats or rabbits when sulcotrione was administered by oral gavage and no neurotoxicity was attributed to sulcotrione administration.

The Acceptable Daily Intake (ADI) was 0.0004 mg/kg bw/day, the Acceptable Operator Exposure (AOEL) was 0.0006 mg/kg bw/day and no Acute Reference Dose (ARfD) was allocated. According to the German model, estimated operator exposure was below the AOEL only if personal protective equipment (PPE) as gloves during mixing/loading and application, and coverall and sturdy footwear during application were worn. Estimated exposure of workers entering crops treated with sulcotrione was below the AOEL, even when no PPE was considered. Bystander's exposure was low compared to the AOEL value.

The metabolism of sulcotrione in maize was investigated after post emergence application reflecting the representative use supported by the applicant. The metabolic degradation of sulcotrione is essentially focused to the cyclohexanedione ring and the formation of CMBA. CMBA was the only significant metabolite formed and only occurs at significant levels in the forage. The meeting of experts PRAPeR 45 agreed that it should be included in the residue definition for risk assessment. However, the animal metabolism study where CMBA was dosed showed that no significant residues will occur. Therefore the risk assessment would not have changed except that the ADI has been lowered. Revised TMDI calculations showed intakes at 31 % of the ADI. As CMBA is a significant but non relevant metabolite in ground water at a level above 0.75 µg/L a consumer risk assessment is required. The risk assessment for CMBA gives a highest intake of <0.2 % of the ADI for CMBA.

An acute risk assessment was not necessary as no ARfD has been set.

The fate and behaviour of sulcotrione in the environment was investigated using phenyl-labelled sulcotrione only, except the phototransformation study in water. The meeting of experts PRAPeR 42 agreed on the need for additional investigation with sulcotrione radiolabelled in the cyclohexanedione ring to finalise an appropriate environmental exposure assessment at the EU level. Therefore data gaps were identified for an aerobic soil degradation study and for a water-sediment study performed with cyclohexanedione-labelled sulcotrione or for evidences to demonstrate that the cyclohexanedione ring of sulcotrione is labile in the environment. For the applied for intended uses, the potential for groundwater exposure by sulcotrione above the parametric drinking water limit of 0.1 µg/L, is low. PEC_{gw} calculations for CMBA indicate that this metabolite has the potential to contaminate groundwater at concentrations above µg/L in 6 out of 8 European FOCUS scenarios The toxicological assessment was able to conclude that CMBA is not relevant regarding groundwater at the expected concentrations.

A potential high long-term risk to birds and mammals was indicated in the first-tier risk assessment. The long-term risk to herbivorous birds was assessed as low taking into account the decline of residues in plants. The suggested PT refinements for insectivorous birds were not sufficiently supported by data and a data gap was identified in the experts` meeting. A new study was submitted by the applicant and a refined risk assessment based on this study was included by the RMS in the not peer-reviewed addendum 3 from May 2008. The long-term risk to mammals was refined by using residue decline data and the new (higher) long-term endpoint agreed in the experts meeting resulting in a TER above the trigger of 5. The risk from uptake of contaminated drinking water and the risk from the major plant metabolite CMBA to birds and mammals were assessed as low.
The TERs for all groups of aquatic organisms were greater than the Annex VI triggers of 100 and 10 except for *Lemna gibba*. One (R4 stream) out of seven FOCUS step 3 scenarios resulted in a TER >10 for *Lemna gibba*. Risk mitigation measures are required under environmental conditions represented by scenario R4. The metabolite CMBA is of low toxicity and risk to aquatic organisms including *Lemna gibba*. The risk to the standard non-target arthropod indicator species was assessed as low. Effects of >50% were observed in tests with *Coccinella septempunctata* and *Pardosa sp* at the suggested application rate of 450 g sulcotrione/ha. The risk to *C. septempunctata* was assessed as low in higher tier (extended laboratory) studies. Significant effects were observed in aged residue tests with Pardosa sp. up to day 42 (after 56 days of ageing of residues no increased mortality was observed). Although the effects were <50% it is uncertain if recolonisation would occur in a real field situation due to the long persistence of effects. No further information was made available to demonstrate recovery/recolonisation of spiders in the in-field area. The LR_{50} for *Pardosa sp*. was calculated as 10.34g a.s./ha which is below the calculated off-field exposure rate of 12.47g a.s./ha indicating a potential high risk for spiders in the off-field area. It was agreed by the experts that risk mitigation measures comparable to a 5m in-field no-spray buffer zone should be applied to ensure that recolonisation of the in-field area is possible from unaffected off-field areas. A potential high risk was identified for non-target plants in the off-field area. Risk mitigation measures comparable to a no-spray buffer zone of 10m is recommended.

The risk to bees, earthworms, soil non-target macro- and micro-organisms and biological methods of sewage treatment were assessed as low for the representative use in maize.

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

- Operator exposure is estimated to be below the AOEL only if personal protective equipment (PPE) as protective gloves during mixing/loading and gloves, protective garment and sturdy footwear during application are worn, according to the German model (refer to point 2.12).
- Risk mitigation measures are required to protect aquatic higher plants under environmental conditions represented by FOCUS step 3 scenario R4.
- Risk mitigation comparable to an in-field no-spray buffer zone of 5m is required to protect sensitive non-target arthropods (spiders) in the off-field area.
- Risk mitigation comparable to an in-field no-spray buffer zone of 10m is required to protect non-target plants in the off-field area.

Critical areas of concern

- The specification for the impurities has not been finalised
- The aerobic degradation route in soil and in water has not been completely finalised as information on the degradation pathway of sulcotrione radiolabelled in the cyclohexanedione ring are not available
- A high long-term risk to insectivorous birds cannot be excluded on the basis of the peer-reviewed data.

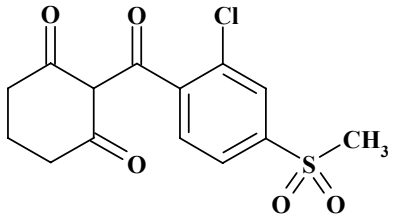
APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

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

Active substance (ISO Common Name) ‡	Sulcotrione (ISO)
Function (*e.g.* fungicide)	Herbicide
Rapporteur Member State	Federal Republic of Germany
Co-rapporteur Member State	–

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	2-(2-chloro-4-mesylbenzoyl)cyclohexane-1,3-dione
Chemical name (CA) ‡	1,3-cyclohexanedione, 2-[2-chloro-4-(methylsulfonyl)benzoyl]-
CIPAC No ‡	723
CAS No ‡	99105-77-8
EC No (EINECS or ELINCS) ‡	not allocated
FAO Specification (including year of publication) ‡	none
Minimum purity of the active substance as manufactured ‡	min. 630 g/kg (on an as received basis (water wet paste)) max. value for the TK: open min. 950 g/kg (on a dry weight basis)
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Hydrogen cyanide maximum content 80 mg/kg on a dry weight basis Toluene maximum content 4 g/kg on a dry weight basis.
Molecular formula ‡	$C_{14} H_{13} Cl O_5 S$
Molecular mass ‡	328.77 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	139 °C (98.8 %)
Boiling point (state purity) ‡	Not measurable, decomposition above 170 °C
Temperature of decomposition (state purity)	170 °C (98.8 %)
Appearance (state purity) ‡	white solid (98.8 %)
Vapour pressure (state temperature, state purity) ‡	$5x10^{-6}$ Pa at 25 °C (extrapolated) (98.8 %)
Henry's law constant ‡	$6x10^{-7}$ Pa m^3 mol^{-1} (calculated for 20 °C and pH 4.8)
Solubility in water (state temperature, state purity and pH) ‡	pH 3.6 (unbuffered): 0.13 g/L at 20 °C (98.8 %)
	pH 4.8 (buffered): 1.67 g/L at 20 °C
	pH 9 (buffered): > 60 g/L at 20 °C
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 20 °C in g/L (99.6 %): n-heptane < 0.1 xylene 2 dichloromethane 190 2-propanol 0.8 1-octanol 0.3 ethylacetate 15 polyethylen glycol (PEG) 23 acetone 48 acetonitrile 55 dimethylsulfoxide 190
Surface tension ‡ (state concentration and temperature, state purity)	69 mN/m at 20 °C (90 % saturated solution) (99.6 %)
Partition co-efficient ‡ (state temperature, pH and purity)	pH 4: log $P_{O/W}$ = 0.2 at 20 °C (99.6 %)
	pH 7: log $P_{O/W}$ = - 1.7 at 20 °C (99.6 %)
	pH 9: log $P_{O/W}$ = - 2.0 at 20 °C (99.6 %)
Dissociation constant (state purity) ‡	pK_a = 3.13 (98.8 %)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	285 nm: ε = 15239 L mol^{-1} cm^{-1} (99.6 %, pH 0.0) 283.5 nm: ε = 16868 L mol^{-1} cm^{-1} (99.6 %, pH 6.4) 259 nm: ε = 20364 L mol^{-1} cm^{-1} (99.6 %, pH 12.6)
Flammability ‡ (state purity)	Not highly flammable in the sense of EC guideline A.10. (71.5 %).

Explosive properties ‡ (state purity)	Sulcotrione is not explosive in the sense of EC guideline A.14 (71.5 %).
Oxidising properties ‡ (state purity)	Sulcotrione has no oxidising properties in the sense of EC guideline A.17 (71.5 %).

Summary of representative uses evaluated (*sulcotrione*)*

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Maize	**EU**	**Mikado**	**F**	**Broad-leaved weeds**	**SC**	**300 g/L**	**overall spray**	**post emer-gence up to BBCH 19**	**1**	**n.a.**	**0.075-0.225**	**200-400**	**0.300-0.450**	**n.a.**	**[1]**

Remarks:
(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
(b) Outdoor or field use (F), glasshouse 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 plants - type of equipment used must be indicated
(i) g/kg or g/L
(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) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

[1] A potential high long-term risk to birds cannot be excluded on the basis of the peer-reviewed data. (a new risk assessment was provided in the not-peer reviewed addendum 2).

Methods of Analysis

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

Technical as (analytical technique)	HPLC-UV
Impurities in technical as (analytical technique)	HPLC-UV GC - FID Photometry (cyanide) Karl-Fischer-Titration
Plant protection product (analytical technique)	HPLC-UV

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		sulcotrione
Food of animal origin		Not relevant, no MRL proposed
Soil		sulcotrione
Water	surface	sulcotrione
	drinking/ground	sulcotrione
Air		sulcotrione

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	LC-MS/MS 0.05 mg/kg (maize, wheat, orange, tomato, olive)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not relevant, no MRL proposed
Soil (analytical technique and LOQ)	LC-MS/MS 0.01 mg/kg (sandy loam) HPLC-UV 0.01 mg/kg (sandy loam)
Water (analytical technique and LOQ)	LC-MS/MS ~~0.1~~ 0.05 µg/L (river water)
Air (analytical technique and LOQ)	In consideration of the AOEL of 0.0006 mg/kg bw/d (proposed by PRAPeR 44) a new method with a LOQ of 0.18 µg/m³ is required.
Body fluids and tissues (analytical technique and LOQ)	Not relevant, not classified as toxic or highly toxic (T/T^+)

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

	RMS/peer review proposal
Active substance	none

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	Rapid and complete (82 – 92 % within 24 hours, based on urinary excretion and intravenous/oral comparison)
Distribution ‡	Poor penetration into tissues, higher concentrations only in liver and kidney
Potential for accumulation ‡	No evidence of accumulation
Rate and extent of excretion ‡	Nearly complete after 96 hours, mainly in the urine (> 90 %)
Metabolism in animals ‡	Generally limited (< 10 % of dose) with the exception of more extensive (> 30 %) metabolism in rat eyes; main pathways: hydroxylation, hydrolysis
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound and CMBA (a plant and soil metabolite occurring in the whole rat organism only in traces of < 1 % but to a rather large amount in the eyes)
Toxicologically relevant compounds ‡ (environment)	Parent compound

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 5000 mg/kg bw	
Rabbit LD_{50} dermal ‡	> 4000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 1.63 mg/L (highest technically available concentration, 4-hour, nose-only exposure)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Non-irritant	
Skin sensitisation ‡	Sensitiser (M&K)	R 43

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Eye damage (corneal opacity, keratitis), liver and kidney effects	
Relevant oral NOAEL ‡	90-day, rat: 3.3 mg/kg bw/day 90-day/1-year, dog (overall NOAEL): 50 mg/kg bw/day	
Relevant dermal NOAEL ‡	28-day, rat: 1000 mg/kg bw/day	
Relevant inhalation NOAEL ‡	No data, not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

	Some positive or equivocal results, mainly *in vitro*, contravened by negative studies. Based on weight of evidence and on the lack of carcinogenicity, no genotoxic risk anticipated.	

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

Target/critical effect ‡	Eye damage (corneal opacity, keratitis), increased kidney weight and chronic progressive nephrosis in rats
Relevant NOAEL ‡	**LOAEL:** 2-year, rat: 0.04 mg/kg bw/day 18-month, mouse: 5.2 mg/kg bw/day
Carcinogenicity ‡	No carcinogenic potential

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Parental: Eye damage, effects on liver and kidneys Reproduction: None Offspring: Decreased pup viability and growth, increased incidence of urinary tract abnormalities	Repr. Cat. 3 R63
Relevant parental NOAEL ‡	0.06 mg/kg bw/day	
Relevant reproductive NOAEL ‡	340 mg/kg bw/day	
Relevant offspring NOAEL ‡	0.6 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Rat: Maternal: Reduced food consumption and body weight gain Developmental: reduced foetal weight and growth retardation Rabbit: Maternal: Reduced food consumption and body weight gain Developmental: None	
Relevant maternal NOAEL ‡	Rat: 100 mg/kg bw/day Rabbit: 100 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 100 mg/kg bw/day Rabbit: 300 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

	No specific studies conducted; evidence for neurotoxicity such as ataxia as part of a general toxic response at high dose levels in subchronic dog studies	
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 ‡	Tyrosinaemia in rats proven at 10 ppm and above. No evidence of eye effects in Rhesus monkeys and rabbits in studies with repeated oral administration. No detection of metabolite CMBA in the eyes of monkeys.
Studies performed on metabolites or impurities ‡	Metabolite CMBA caused severe eye irritation but showed low toxicity in acute (oral, dermal, inhalation), subacute, subchronic and reproduction studies and proved negative for genotoxicity (tested *in vitro* only) – Proposed ADI: 0.2 mg/kg bw/day (90-day oral rat and 1-generation rat) applying a safety factor of 1000 due to the limited data base.

Medical data ‡ (Annex IIA, point 5.9)

No adverse effects in plant personnel or agricultural operators reported so far

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.0004 mg/kg bw/day	2-year rat	100*
AOEL ‡	0.0006 mg/kg bw/day	Rat, multigeneration	100
ARfD ‡	Not allocated, not necessary (no acute toxicological alerts)		

*ADI derived from a LOAEL but higher safety factor not necessary based on steep dose response curve

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation MIKADO (300 g sulcotrione/L SC)	0.1 % concentrate, 0.5 % dilution (based on human *in vitro* data)

Exposure scenarios (Annex IIIA, point 7.2)

Operator	The estimated exposure for MIKADO according to the German model (application rate in maize 0.45 kg sulcotrione/ha) was below the AOEL only if PPE are worn; according to the UK POEM, exposure is above the AOEL even if PPE are worn. German model: % of AOEL without PPE 304 % PPE (gloves during mixing/loading and application and coverall during application) 50.2 % UK-POEM: % of AOEL without PPE: 1797 % PPE (gloves during mixing/loading and application) 583 %
Workers	The estimated exposure for MIKADO is below the AOEL even when no PPE are worn according to Hoernicke E. *et. al*. 1998 No PPE 75 % of the AOEL
Bystanders	The estimated exposure for MIKADO is below the AOEL according to Ganzelmeier *et. al*. (2000) drift data and German model inhalation data Exposure 5.45 % of the AOEL

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

	RMS/peer review proposal
Sulcotrione	Xn, Reproduction Cat. 3, R63 (Possible risk of harm to the unborn child); R43 (May cause sensitisation by skin contact)

Residues

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

Plant groups covered	Maize
Rotational crops	Not necessary
Metabolism in rotational crops similar to metabolism in primary crops?	
Processed commodities	
Residue pattern in processed commodities similar to residue pattern in raw commodities?	
Plant residue definition for monitoring	Sulcotrione
Plant residue definition for risk assessment	Sum of Sulcotrione and CMBA, expressed as Sulcotrione
Conversion factor (monitoring to risk assessment)	None (CMBA has no impact on the risk assessment)

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

Animals covered	Goat
Time needed to reach a plateau concentration in milk and eggs	
Animal residue definition for monitoring	Not necessary
Animal residue definition for risk assessment	Not necessary
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No

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

Not necessary

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

Sulcotrione: maize (fodder, grain) 730 days
CMBA: maize (fodder, grain) 730 days

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)	Ruminant: no	Poultry: no	Pig: no
Potential for accumulation (yes/no):			
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)			
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle			
Liver			
Kidney			
Fat			
Milk			
Eggs			

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Maize	Northern	Grain: Sulcotrione: < 0.05(10) mg/kg CMBA: < 0.05(10) mg/kg			0.05	0.05
	Mediterranean	Grain: Sulcotrione: < 0.05(10) mg/kg CMBA: < 0.05(10) mg/kg				
Sweet Corn	Northern	No trials			0.05	0.05
	Mediterranean	Grain: Sulcotrione: < 0.05(3) mg/kg CMBA: < 0.05(3) mg/kg				

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

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

ADI	Sulcotrione 0.0004 mg/kg bw/day CMBA[13] 0.2 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	31 cluster B, CMBA for water intake <0.2
TMDI (% ADI) according to national (to be specified) diets	31 IE-diet
IEDI (WHO European Diet) (% ADI)	Not calculated
NEDI (specify diet) (% ADI)	Not calculated
Factors included in IEDI and NEDI	
ARfD	Not allocated
IESTI (% ARfD)	Not applicable
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Not applicable
Factors included in IESTI and NESTI	

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	
No Processing available				

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

Maize	0.05 mg/kg

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

[13] CMBA: 2-chloro-4-(methylsulfonyl)-benzoic acid

Fate and behaviour in the environment

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

Mineralisation after 100 days ‡	silt loam - application rate: 1 ppm, 25 °C 58.3 % AR after 120 d, [phenyl-UL-14C]-label (study end) - application rate: 1 ppm, 5 °C 2.9 % AR after 120 d, [phenyl-UL-14C]-label (study end) - application rate: 100 ppm, 25 °C 2.5 % AR after 120 d, [phenyl-UL-14C]-label (study end) Sterile conditions: 0 % AR after 120 d Sand, application rate: 1 ppm, 25 °C 73.8 % AR after 120 d, [phenyl-UL-14C]-label (study end) Sandy loam - application rate: 1 ppm, 25 °C 2.7% AR after 120 d, [phenyl-UL-14C]-label (study end)

Non-extractable residues after 100 days ‡	silt loam - application rate 1 ppm, 25 °C 26.5 % AR after 120 d, [phenyl-UL-14C]-label (study end) - application rate: 1 ppm, 5 °C 12.3 % AR after 120 d, [phenyl-UL-14C]-label (study end) - application rate: 100 ppm, 25 °C 17.6 % AR after 120 d, [phenyl-UL-14C]-label (study end) Sterile conditions: 17.3 % AR after 120 d Sand - application rate: 1 ppm, 25 °C 5.9 % AR after 120 d, [phenyl-UL-14C]-label (study end) Sandy loam - application rate: 1 ppm, 25 °C 15.2 % AR after 120 d, [phenyl-UL-14C]-label (study end)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	CMBA (M01) Silt loam - application rate 1 ppm, 25°C: max. 28.7 % AR after 30 days - application rate 1 ppm, 5 °C: max. 16.2 % AR after 120 days - application rate 100 ppm, 25°C: max. 60.3 % AR after 120 days (end of the study) Sand - application rate 1 ppm, 25°C: max. 47.5 % AR after 21 days Sandy loam - application rate 1 ppm, 25°C max. 39.5 % AR after 120 days % (end of the study) An aerobic soil degradation study performed with sulcotrione radiolabelled in the cyclohexanedione-ring or evidences to demonstrate that potential metabolites containing the cyclohexanedione ring are labile are required (**data gap** identified by meeting of experts PRAPeR 42).

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

Anaerobic degradation ‡	
Mineralisation after 100 days	13.8 % AR after 90 d (anaerobic; = 102 d including aerobic pre-incubation), [phenyl-UL-14C]-label 8.5 % AR after 120 d (anaerobic; = 132 d including aerobic pre-incubation), [phenyl-UL-14C]-label Sterile conditions: not applicable silt soil tested: sand: 8.5 % silt: 81.3 % clay: 10.2 % organic matter:3.63 % pH: 6.7 (CaCl2) application rate: 1 ppm, 25 °C
Non-extractable residues after 100 days	13.9 % AR after 90 d (anaerobic; 102 d including aerobic pre-incubation), [phenyl-UL-14C]-label 14.6 % AR after 120 d (anaerobic; 132 d including aerobic pre-incubation), [phenyl-UL-14C]-label
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	CMBA (M01) 53.2 – 60 % AR at 120-30 d (max at day 30) [phenyl-UL-14C]-label
Soil photolysis ‡	Investigated: [Phenyl-UL-^{14}C] sulcotrione in silt, 75 % WHC, 1/3 bar, 20 °C Continuous irradiation (irradiation cabinet ® Suntest, Heraeus Original Hanau, 6.39 MJ*m^{-2} * h^{-1}) for 8 d CO_2 not detected bound residues not detected metabolites max 24.6 % AR, d 7 DT_{50} 18.3 d
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	CMBA (M01) 4.0 – 24.6 % AR at 0.25-7 d (max at day 7) [phenyl-UL-^{14}C]-label

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

Laboratory studies ‡

Parent	Aerobic conditions						
Soil type	X14	pH	t. °C / % MWHC	DT50 /DT90 (d)	DT50 (d) 20 °C pF2/10kPa	St. (r2)	Method of calculation
silt loam (Iowa)	CaCl2	5.6	25 °C/75 % FC	24.0/79.7	29.1	0.979	SFO
silt loam (Iowa)	CaCl2	5.6	5 °C/75 % FC	137	no data submitted and not relevant	no data submitted and not relevant	1st order, TF
sand (Toulouse)	CaCl2	5.2	25 °C/75 % FC	15.0/49.8	18.2	0.967	SFO
sandy loam (San Jose)	CaCl2	7.3	25 °C/75 % FC	74.0/245.9[1)]	89.7	0.989	SFO
loamy sand (Speyer 2.2)	CaCl2	5.9	20 °C/40 % MWHC	14.1/47	10.8	0.993	SFO
sand (East Anglia)	CaCl2	8.0	20 °C/40 % MWHC	23.6/78.4	20.2	0.985	SFO
Geometric mean/median				24.2 (DT50, TF, geom. mean) 24.5 (DT50, SFO, geom. mean)	25.3 geom. mean)		

[1)] DT_{50} and DT_{90} worst case

Met CMBA	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
silt loam (Iowa)	$CaCl_2$	5.6	25 °C/75 % FC	72 23.1/n.a.	0.7	28.1	0.979	1st order, TF SFO
sand (Toulouse)	$CaCl_2$	5.2	25 °C/75 % FC	48 28.1/n.a.	0.81	34.1	0.967	1st order, TF SFO

[14] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Met CMBA	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
sandy loam (San Jose)	$CaCl_2$	7.3	25 °C/75 % FC	"increase"				
loamy sand (Speyer 2.2)	$CaCl_2$	5.9	20 °C/40 % MWHC	12.2/n.a.	0.22	9.4	0.993	SFO
sand (East Anglia)	$CaCl_2$	8.0	20 °C/40 % MWHC	44.8/n.a.	0.22	38.3	0.985	SFO
Geometric mean/median				**24.4** (geometric mean)	**0.49** (arithm. mean) **0.41** (geom. nean)	**24.2** (geometric mean)		

n.a. = not available

Field studies ‡

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X[1]	pH No specification	Depth (cm)	DT_{50}/ DT_{90} (d) actual	DT_{50}(d) Norm.	DT_{90} (d) Norm.	St. (chi^2) Norm.	Method of calculation
Sandy / clay loam cropped	South France Grisolles	none	8.1	0-20	8.7/5.3	1.2	4.0	14.4	SFO / norm
coarse sand cropped	South France Ychoux	none	6.2	0-20	3.6/60.6 (FOMC)[4] 18.3 (SFO)*	8.9*	29.3	2.5	FOMC / norm
clay cropped	Italy Emilia Romagna	none	8.1	0-20	2.4/45.7 (FOMC)[5] 13.8 (SFO)*	10.3*[3]	34.1	11.2	FOMC/ norm

Field studies ‡

Parent	Aerobic conditions								
loam cropped	Italy Lombardia	none	7.8	0-20	2.5/14.9 (FOMC)[6] 4.7 (SFO)*	2.2[3]	7.4	10.1	FOMC/ norm
sandy loam bare	Italy Veneto	none	7.3	0-20	16.5/54.3	11.4[3]	38	17.5	SFO / norm
loamy sand bare	Germany Bienenbüttel-Varendorf	none	6.1	0-10	4.7/28.8 (FOMC)[7] 8.7 (SFO)*	2.1	6.9	10.5	SFO / norm
sandy loam bare	Germany Klein-Zecher	none	6.1	0-10	11.1/36.9	5.3	17.6	7.5	SFO / norm
clay bare	Germany Ottersweiher-Unzurst	none	5.3	0-30	9.9/32.9	5.2	17.2	8.9	SFO / norm
clay loam bare	Germany Sollern	none	6.8	0-30	6.5/21.4	3.4	11.3	7.5	SFO / norm
Geometric mean/median **Geometric mean/median for FOCUS Modelling**					**10.1/9.9**	**3.6/4.3**			SFO

*) back-calculated from DT90 as conservative DT50 estimate for modelling
3) not considered for PEC_{GW}
4) alpha= 0.662, beta= 1.928, P ini= 0.395
5) alpha= 0.630, beta= 1.218, P ini= 0.290
6) alpha= 1.622, beta= 4.723, P ini= 0.269
7) alpha= 1.539, beta= 8.323, P ini= 0.259

Met CMBA	Aerobic conditions								
Soil type	Location	X[1]	pH	Depth (cm)	DT_{50} (d) actual	DT_{50} (d) Norm.	DT_{90} (d) Norm.	St. (chi^2) Norm.	Method of calculation
Sandy / clay loam	South France	none	8.1	0-20	n.a.	4.9	16.3	14.8	SFO / norm
coarse sand	South France	none	6.2	0-20	n.a.	34.7	115.1	16.3	SFO / norm

Met CMBA	Aerobic conditions								
clay	Italy	none	8.1	0-20	n.a.	45.4[3]	150.8	14	SFO / norm
loam	Italy	none	7.8	0-20	n.a.	42.8[3]	142	17.2	SFO / norm
sandy loam	Italy	none	7.3	0-20	n.a.	25.6[3]	85	7.4	SFO / norm
loamy sand	Germany	none	6.1	0-10	n.a.	10.6	35.5	7.8	SFO / norm
sandy loam	Germany	none	6.1	0-10	n.a.	2.5	8.4	4.8	SFO / norm
clay	Germany	none	5.3	0-30	n.a.	30.5	101.5	12.5	SFO / norm
clay loam	Germany	none	6.8	0-30	n.a.	2.8	9.2	8.2	SFO / norm
Geometric mean/median						**8.5/ 7.8**			
formation fraction / mean					**62.1%**			-	

n.a. = not available
3) not considered for PEC_{GW}

pH dependence ‡ (yes / no) (if yes type of dependence)	no
Soil accumulation and plateau concentration ‡	not applicable

Laboratory studies ‡

Parent	Anaerobic conditions						
Soil type	X[15]	pH $CaCl_2$	t. °C / % MWHC	DT_{50} / DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
silt 12 days aerobic, 120 days anaerobic incubation		6.7	20	stable	-	-	-
Geometric mean/median							

[15] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Met 1	Anaerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
no data submitted								
Geometric mean/median								

Soil adsorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH	K_f (mL/g)	$K_{f,oc}$ (mL/g)	K_d (mL/g)	$K_{d,oc}$ (mL/g)	1/n
Little Shelford, sandy loam	1.5	7.2	0.29	19			0.835
Flint Hall, clay loam	2.9	7.1	0.50	17			0.812
Shelley Field, clay loam	1.9	7.1	0.79	41			0.888
Calke, sandy loam	3.9	5.5	2.26	58			0.837
Lockington, sandy clay	3.3	6.3	1.42	43			0.824
Arithmetic mean (adsorption)			**1.05**	**36**			**0.839**
pH dependence, Yes or No				yes (predominantly OC-dependence, pH-dependence to a minor extend)			

Metabolite CMBA ‡							
Soil Type	OC %	Soil pH	K_f (mL/g)	$K_{f,oc}$ (mL/g)	K_d (mL/g)	$K_{d,oc}$ (mL/g)	1/n
Toulouse, sand	0.81	5.2	0.05	6.60			0.925
San Jose, sandy loam	0.17	7.3	0.02	8.98			0.873
Iowa, silt loam	2.44	5.6	0.04	1.82			0.869
Luling, clay loam	1.04	7.5	0.01	1.08			0.708
Velizy, sandy loam	3.83	4.9	0.20	5.30			0.931
Arithmetic mean (adsorption)			0.064	4.76			0.861
pH dependence (yes or no)			yes (predominantly OC-dependence, pH-dependence to a minor extend)				

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

Column leaching ‡

application rate: 750 g/ha

soils:

Sorrento loam (Sand: 43.2 %, pH: 6.7)
San Jose Sandy loam (Sand: 61.2 %, pH: 7.3)
St. John's Sand (Sand: 91.6 %, pH: 5.1)
Bigg's Clay (Sand: 22.8 %, pH: 5.5)

Irrigation: 505 mm

	Water loading period	Leachates	Soil
Sorrento	6 d	84.0 ± 1.0	16.0 ± 1.0
San Jose	8 – 10 h	97.9 ± 0.1	2.1 ± 0.1
St. John's	8 – 10 h	6.7 ± 0.2	93.3 ± 0.2
Bigg's	8 – 10 h	8.7 ± 2.1	91.3 ± 2.1

Percent distribution of radioactivity in sulcotrione and its metabolite formed in soil column segments and leachates

Soil/column	Fraction	C^{14} in metabolites [%] sulcotrione	CMBA
Sulcotrione	standard	94.3	1.5
Sorrento, 1S	leachate	97.3	0.8
San Jose, 3S	leachate	98.1	0.0
St. John's, 5S-1	0-6 cm soil	78.0	21.7
5S-6	30-36 cm soil	71.4	27.8
Bigg's 7S-1	0-6 cm soil	90.3	8.6
7S-6	30-36 cm soil	78.2	18.2

Aged residues leaching ‡: not applicable

Lysimeter/ field leaching studies ‡: not applicable

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

DT_{50} (d): 16.5 days[16]

Method of calculation

Field or Lab: non-normalised maximum field-

[16] Value not considered reliable, but accepted for PECsoil calculations as it represents a worst case.

Application data	Crop: maize Depth of soil layer: (eg. 5 cm, 20 cm). 25 % plant interception: Number of applications: 1 Interval (d): - Application rate(s): 450 g as/ha

PEC(s) (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.450		Not relevant	Not relevant
Short term	24h	0.432	0.440		
	2d	0.414	0.432		
	4d	0.380	0.414		
Long term	7d	0.335	0.389		
	28d	0.139	0.265		
	50d	0.055	0.18		
	100d	0.007	0.105		
Plateau concentrations		Not relevant			

Metabolite CMBA Method of calculation	Molecular weight:-235 g/mol DT_{50} (d): 38.3 days[17] Field or Lab normalised maximum from lab studies.
Application data	Application rate assumed: 450 g as/ha (assumed Met I is formed at a maximum formation rate (laboratory) of 81% of the applied dose)

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.1390			
Short term	24 h	0.1390	0.1390		
	2 d	0.1388	0.1390		
	4 d	0.1383	0.1389		
Long term	7 d	0.1369	0.1388		
	28 d	0.1149	0.1356		

[17] Value not considered reliable, but accepted for PECsoil calculations as it represents a worst case.

50 d 100 d	0.0862 0.0385	0.1290 0.1073		
Plateau concentration	Not relevant			

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	hydrolytically stable at 25 °C and 40 °C (pH: 5, 7 and 9)
Photolytic degradation of active substance and metabolites above 10 % ‡	Simulation environmental half-life, direct phototransformation in aqueous solution. Model: Frank / Klöpffer; natural surface water (Neckar); concentration: 1 * 10^{-7} mol/L; depth: 5 and 30 cm. Mean DT_{50}: (SFO, mid-European sunlight conditions):

		spring	summer	autumn	winter
pH 4	5 cm	4.4	2.0	3.9	42
	30 cm	7.5	6.4	10	110
pH 7	5 cm	8.7	4.0	7.8	82
	30 cm	15	13	20	210
pH 9	5 cm	14	6.6	13	130
	30 cm	24	21	33	340

Quantum yield of direct phototransformation in water at Σ > 290 nm	$6.3 \cdot 10^{-4}$ mol · Einstein $^{-1}$ (pH 4) $2.9 \cdot 10^{-4}$ mol · Einstein $^{-1}$ (pH 7) $1.7 \cdot 10^{-4}$ mol · Einstein $^{-1}$ (pH 9)
Readily biodegradable ‡ (yes/no)	No, substance considered not ready biodegradable.

Degradation in water / sediment

Parent [phenyl-UL-14C]-label	Distribution (e.g. max in water 90% AR after 0 d. Max. sed. 49.8 % AR after 30 d)									
Water / sediment system	pH water phase	pH sed.	t. °C	DT_{50} - DT_{90} whole sys.	St. (r^2)	DT_{50} - DT_{90} water	St. (r^2)	DT_{50} - DT_{90} sed.	St. (r^2)	Method of calculation
Virgina Water, system 1	no data submitted - not relevant	6.1	13	48 / 159[1)]	0.98	15 / 75 20.2 / 67.1	0.98 0.977	Not evaluated		lin. reg., 1st order; SFO
Old Basing, system 2	no data submitted - not relevant	7.3	11	84 / 278[1)]	1.0	6 / not applicable 41.3 / 137 8.01 / 218.3	0.986 0.765	Not evaluated		lin. reg., 1st order; Mathcad, 1st order Mathcad best fit
Geometric mean/median				63.9		9.5				linear regression

[1]) projected from data up to 100 days.

Metabolite CMBA	Distribution (e.g. max in water 42.2% AR after 100 d. Max. sed. 18.6 % AR after 100 d)									
Water / sediment system	pH water phase	pH sed.	t. °C	DT_{50} - DT_{90} whole sys.	St. (r^2)	DT_{50} - DT_{90} water	r^2	DT_{50} - DT_{90} sed.	St. (r^2)	Method of calculation
Virgina Water, system 1	no data submitted - not relevant	6.1	13	no data submitted - not relevant	not relevant	no data submitted - not relevant	not relevant	no data submitted - not relevant	not relevant	Not evaluated

Old Basing, system 2	no data submitted - not relevant	7.3	11	no data submitted - not relevant	not relevant	no data submitted - not relevant	not relevant	no data submitted - not relevant	not relevant	Not evaluated
Geometric mean/median				no data submitted - not relevant		no data submitted - not relevant		no data submitted - not relevant		

Mineralisation and non extractable residues					
Water / sediment system	pH water phase	pH sed.	Mineralisation x % after n d (end of the study)	Non-extractable residues in sed. max x % after n d	Non-extractable residues in sed. max x % after n d (end of the study)
Virgina Water, system 1	no data submitted - not relevant	6.1	6 % CO_2-formation (day 100)	6 (day 100)	6 (day 100 = end of the study)
Old Basing, system 2	no data submitted - not relevant	7.3	4 % CO_2-formation (day 100)	9 (day 100)	9 (day 100 = end of the study)

An additional water-sediment study performed with sulcotrione radiolabelled in the cyclohexanedione-ring or evidences to demonstrate that potential metabolites containing the cyclohexanedione ring are labile are required (**data gap** identified by meeting of experts PRAPeR 42).

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

Parent Parameters used in $FOCUS_{sw}$ step 1 and 2	Molecular weight (g/mol): 329 Water solubility (mg/L): > 60 g/L (pH 9) Kom (L/kg): 21 DT50 soil (d): 4.3 days (geometric mean, field, in accordance with FOCUS-Kinetics, SFO) DT50 water/sediment system (d): 64 (geometric mean; total system) DT50 water (d): 64 (geometric mean; total system) DT50 sediment (d): 999 (worst case) Crop interception (%): 25 % (FOCUS step 2)
Parameters used in $FOCUS_{sw}$ step 3 (if performed)	Vapour pressure: 5 10-6 Pa Kom: 21

	1/n: 0.84 (Freundlich exponent general or for soil ,susp. solids or sediment respectively)
Application rate	Crop: maize Crop interception: 25 % (FOCUS Step 2) Number of applications: 1 Interval (d): none Application rate(s): 450 g as/ha Depth of water body: 30 cm Application window: 14 days after emergence
Main routes of entry	2.759 % drift from 1 meter 2 – 5 % runoff/drainage (at FOCUSsw Step 2)

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
R1	Pond	0 h	0.10		0.15	
R1	Stream	0 h	4.11		0.58	
R2	Stream	0 h	2.52		0.39	
R3	Stream	0 h	2.31		0.26	
D3	Ditch	0 h	2.36		0.41	
D4	Pond	0 h	0.10		0.13	
D4	Stream	0 h	1.99		0.08	
D5	Pond	0 h	0.10		0.12	
D5	Stream	0 h	2.01		0.05	
D6	Ditch	0h	2.40		0.53	
R4	Stream	0 h	11.13		1.92	
		24 h	0.069	8.385	0.933	1.54
		2 d	0.004	4.204	0.706	1.24
		4 d	0.001	2.103	0.52	0.94
		7 d	0.000	1.202	0.41	0.75
		14 d	0.000	0.634	0.32	0.57
		21 d	0.017	0.438	0.25	0.47
		28 d	0.000	0.328	0.21	0.41
		42 d	0.000	0.219	0.163	0.34

Metabolite 01 = CMBA Parameters used in FOCUSsw step 1 and 2	Molecular weight: 235 g/mol Water solubility (mg/L): 60000 mg/L Soil or water metabolite: soil and water Kom (L/kg): 3 DT50 soil (d): 13.9 days (geom.. mean field) DT50 water/sediment system (d): 999 (representative worst case from sediment water studies) DT50 water (d): 999 DT50 sediment (d): 999 Crop interception (%): 25 Maximum occurrence observed (% molar basis with respect to the parent) Soil: 62 Water/Sediment: 61
Application rate	Crop: maize Number of applications: 1 Interval (d): - Application rate(s): 450 g as/ha Depth of water body: 30 cm Application window: 14 days after emergence
Main routes of entry	2.759 % drift from 1 meter 2 – 5 % runoff/drainage (at FOCUSsw Step 1 and 2)

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Metabolite CMBA Southern EU (worst case)	0 h				
	4 h	17.99	17.99	0.93	0.93
	d	17.97	17.99	0.93	0.93
	d	17.95	17.97	0.93	0.93
	d	17.91	17.96	0.93	0.93
	4 d	17.83	17.91	0.92	0.93
	1 d	17.74	17.87	0.92	0.92
	8 d	17.65	17.83	0.91	0.92
	42 d	17.48	17.74	0.90	0.92

PEC ground water (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUSgw modelling, values used – Modelling using FOCUS model(s), with appropriate FOCUS gw scenarios, according to FOCUS guidance. Model(s) used: FOCUS PEARL Scenarios (list of names): Châteaudun, Hamburg, Kremsmünster, Okehampton, Piacenza, Porto, Sevilla, Thiva Crop: maize Geometric mean or median parent DT50lab/field: 4.3 d (normalisation to 10 kPa or pF2, 20 °C with Q10 of 2.2). Kom: parent, geometric mean or median 21, 1/n= 84. Metabolite CMBA: Geometric mean DT50 field: 13.9 d (normalisation to 10 kPa or pF2, 20 °C with Q10 of 2.2). Formation fraction: 62 % Kom: geometric mean or median 3, 1/n= 0.861
Application rate	Dates of application : 2 weeks post emergence (From March 7th to May 25th) Crop : Interception estimated: 25% Number of applications: 26, 1 application per year Application rate: 450 g/ha/year

PEC_{gw} - FOCUS modelling results (80^{th} percentile annual average concentration at 1 m)

Model / Crop	Scenario	Parent (µg/L)	Metabolite CMBA (µg/L)		
			1	2	3
	Chateaudun	< 0.001	0.474		
	Hamburg	< 0.001	1.462		
	Kremsmunster	< 0.001	0.741		
	Okehampton	< 0.001	1.085		
	Piacenza	< 0.001	0.625		
	Porto	< 0.001	0.015		
	Sevilla	< 0.001	0.024		
	Thiva	< 0.001	0.385		

A **data gap** was identified by the PRAPeR 42 meeting regarding potential degradation products (e.g. 1,3-cyclohexanedione) containing the cyclohexanedione ring of the molecule.

PEC$_{(gw)}$ From lysimeter / field studies

Parent	1st year	2nd year	3rd year
Annual average (µg/L)	No data provided - none requested		

Metabolite X	1st year	2nd year	3rd year
Annual average (µg/L)	No data provided - none requested		

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

Direct photolysis in air ‡	Not studied
Quantum yield of direct phototransformation	No data submitted - justification accepted
Photochemical oxidative degradation in air ‡	DT50 of 12 hours derived by the Atkinson method of calculation: 1.424 d
Volatilisation ‡	From plant surfaces (BBA guideline): negligible after 24 hours
	From soil surfaces (BBA guideline): negligible after 24 hours
	From water: vapor pressure = 3 * 10-6 Pa (20 °C) Henry´s Law constant H = 6 * 10-7 Pa m3 mol-1 (pH 4.8, 20 °C) volatilisation from water negligible
Metabolites	no potentially volatile metabolites

PEC$_{air}$

Method of calculation	Expert judgement, based on vapour pressure, dimensionless Henry's Law Constant and information on volatilisation from plants and soil.

PEC$_{(a)}$

Maximum concentration	e.g. negligible

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology). (> 10 % of as or > 5 % of as in 2 sequential measurements)	Soil: sulcotrione, CMBA (data gap regarding potential degradation products (e.g. 1,3-cyclohexanedione) containing the cyclohexanedione ring of the molecule) Surface Water: sulcotrione, CMBA (data gap regarding potential degradation products (e.g. 1,3-cyclohexanedione) containing the cyclohexanedione ring of the molecule) Ground water: sulcotrione, CMBA (data gap regarding potential degradation products (e.g. 1,3-cyclohexanedione) containing the cyclohexanedione ring of the molecule) Air: sulcotrione

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

*) If direct photolysis data is provided, information on the latitude etc. should be included

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

R53	May cause long-term adverse effects in the aquatic environment (not readily biodegradable)

Ecotoxicology

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

Species	Test substance	Time scale	Endpoint (mg/kg bw/day)	Endpoint (mg/kg feed)
Birds ‡				
Anas platyrhynchos	Sulcotrione	Acute	LD_{50} > 1350	Not relevant
	Preparation	Acute	No data submitted – justification accepted	
	Metabolite CMBA	Acute		
Anas platyrhynchos	Sulcotrione	Short-term	LD_{50} > 1259	LD_{50} > 5620
Anas platyrhynchos	Metabolite CMBA	Short-term	LD_{50} > 2010	LD_{50} > 5000
Anas platyrhynchos	Sulcotrione	Long-term, 6-week feeding study, reproduction	NOEL 17	NOEC 111
Anas platyrhynchos	Sulcotrione	Long-term, 20-week feeding study, bw of chicks	NOEL < 10.9	NOEC < 89
Mammals ‡				
Rat	Sulcotrione	Acute	LD_{50} > 5000	Not relevant
Rat	Preparation	Acute	LD_{50} > 2000	Not relevant
Rat	Metabolite CMBA	Acute	LD_{50} > 2000	Not relevant
Rat	Sulcotrione	Long-term, 2-generation	NOEL 0.5	NOEC 10
Rat	Metabolite CMBA	Long-term, males 1-generation reproduction	NOEL 969	NOEC 10000
Additional higher tier studies ‡				
No data submitted – justification accepted				

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

Crop and application rate

Indicator species/Category[2]	Time scale		ETE	TER1	Annex VI Trigger[3]
Tier 1 (Birds)					
Medium herbivorous birds	Acute	Sulcotrione	29.75	> 45	10
Insectivorous birds	Acute	Sulcotrione	24.34	> 56	10

Indicator species/Category[2]	Time scale	ETE	TER1	Annex VI Trigger[3]
Medium herbivorous birds	Short-term Sulcotrione	13.68	> 92	10
Medium herbivorous birds	Short-term	13.68	> 147	10
Insectivorous birds	Short-term Sulcotrione	13.57	> 92	10
Insectivorous birds	Short-term Met. CMBA	13.57	> 148	10
Medium herbivorous birds	Long-term Sulcotrione	7.25	< 1.5	5
Insectivorous birds	Long-term Sulcotrione	13.57	< 0.8	5
Higher tier refinement (Birds)				
Medium herbivorous birds	Long-term Sulcotrione	0.094	181*	10
* ftwa = 0.00687 due to DT50 0.1 day				
Tier 1 (Mammals)				
Medium herbivorous mammal	Acute Sulcotrione	10.96	> 456	10
Medium herbivorous mammal	Acute Met. CMBA	10.96	> 182	10
Medium herbivorous mammal	Long-term Sulcotrione	2.67	0.187	5
Medium herbivorous mammal	Long-term Met. CMBA	2.67	363	5
Higher tier refinement (Mammals)				
Medium herbivorous mammal	Long-term Sulcotrione	0.0035	14 ftwa 0.0069 ~~4.4~~	5

[1] in higher tier refinement provide brief details of any refinements used (e.g. residues, PT, PD or AV)
[2] for cereals indicate if it is early or late crop stage
[3] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

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

Group	Test substance	Time-scale (Test type)	Endpoint	Toxicity[1] (mg/L)
Laboratory tests ‡				
Fish				
Oncorhynchus mykiss	Sulcotrione	96 hr (static)	Mortality, EC50	227 mm
Oncorhynchus mykiss	Sulcotrione	28 d (semi-static)	Juvenile growth NOEC	3.2 nom
Oncorhynchus mykiss	Preparation	96 hr (static)	Mortality, EC_{50}	100 as nom 390 product
Oncorhynchus mykiss	Preparation	28 d (flow-through)	Growth NOEC	Not relevant
Oncorhynchus mykiss	Metabolite CMBA	96 hr (static)	Mortality, EC_{50}	> 180 nom
Oncorhynchus mykiss	Metabolite CMBA	28 d (semi-static)	Juvenile growth NOEC	≥ 120 nom
Aquatic invertebrate				
Oncorhynchus mykiss	Sulcotrione	96 hr (static)	Mortality, EC_{50}	227 mm
Oncorhynchus mykiss	Sulcotrione	28 d (semi-static)	Juvenile growth NOEC	3.2 nom
Oncorhynchus mykiss	Preparation	96 hr (static)	Mortality, EC_{50}	100 as nom 390 product
Oncorhynchus mykiss	Preparation	28 d (flow-through)	Growth NOEC	Not relevant
Oncorhynchus mykiss	Metabolite CMBA	96 hr (static)	Mortality, EC_{50}	> 180 nom
Oncorhynchus mykiss	Metabolite CMBA	28 d (semi-static)	Juvenile growth NOEC	≥ 120 nom
Sediment dwelling organisms				
Chironomus riparius	Sulcotrione	28 d (static)	NOEC	Not relevant
Chironomus riparius	Metabolite CMBA	28 d (static)	NOEC	Not relevant

Group	Test substance	Time-scale (Test type)	Endpoint	Toxicity[1] (mg/L)
Algae				
Selenastrum capricornutum	Sulcotrione	96 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	1.2 nom 3.5 nom
Anabaena flos-aquae	Sulcotrione	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	22 nom 54 nom
Selenastrum capricornutum	Preparation	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.67 as nom 2.5 product 2.7 as nom 10 product
Pseudokirchneriella subcapitata	Metabolite CMBA	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	33 nom 34 nom
Higher plant				
Lemna gibba	Sulcotrione	7 d (static)	Fronds, final biomass E_bC_{50}	0.051 mm
Lemna gibba	Preparation	7 d (static)	Fronds, growth rate E_rC_{50}	0.072 as nom 0.27 product
Lemna gibba	Metabolite CMBA	7 d (static)	Fronds, $E_{r,b}C_{50}$	> 100 mm
Microcosm or mesocosm tests				
Not required, not relevant				

[1] indicate whether based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$). In the case of preparations indicate whether endpoints are presented as units of preparation or as

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

FOCUS Step 1

Maize, 0.45 kg as/ha

Test substance	Organism	Toxicity endpoint (mg/L)	Time scale	PEC_i	PEC_{twa}	TER	Annex VI Trigger[1]
No data submitted - not relevant; justification accepted							

[1] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.
[2] only required for herbicides
[3] consider the need for PEC_{sw} and PEC_{sed} and indicate which has been used

FOCUS Step 2

Maize, 0.45 kg as/ha, post-emergence up to BBCH 19, Southern Europe = worst case

Test substance	N/S[1]	Organism[2]	Toxicity endpoint (mg/L)	Time scale	PEC[3]	TER	Annex VI Trigger[4]
Sulcotrione	S	Fish	227	Acute	26.37	8608	100
Sulcotrione	S	Fish	3.2	Chronic	26.37	121	10
Sulcotrione	S	Aquatic invertebrates	> 848	Acute	26.37	32158	100
Sulcotrione	S	Aquatic invertebrates	75	Chronic	26.37	2844	10
Sulcotrione	S	Algae	1.2	Chronic	26.37	45.5	10
Sulcotrione	S	Higher plants[5]	0.051	Chronic	26.37	**1.9**	10
Sulcotrione	S	Sediment-dwelling organisms[6]	Not relevant	Chronic			10
Metabolites CMBA	S	Algae	33	Chronic	18.00	1833	10
Product	S	Higher plants[5]	0.072 (as)	Chronic	26.37 (as)	**2.7**	10

[1] indicate whether Northern of Southern
[2] include critical groups which fail at Step 1.
[3] indicate whether maximum or twa values have been used.
[4] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.
[5] only required for herbicides
[6] consider the need for PEC_{sw} and PEC_{sed} and indicate which has been used

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Maize, 0.45 kg as/ha

Test substance	Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity endpoint (mg/L)	PEC[4]	TER	Annex VI trigger[5]
Sulcotrione	R1	Pond	Higher plants	chronic	0.051	0.10	510	10
	R1	Stream			(as)	4.11	12	
	R2	Stream				2.52	20	
	R3	Stream				2.31	22	

	D3	Ditch				2.36	22	
	D4	Pond				0.10	510	
	D4	Stream				1.99	26	
	D5	Pond				0.10	510	
	D5	Stream				2.01	25	
	D6	Ditch				2.40	21	
	R4	Stream				11.13	4.6	

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

FOCUS Step 4

Not relevant.

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity endpoint	Buffer zone distance	PEC[4]	TER	Annex VI trigger[5]

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

Bioconcentration

	Active substance	Metabolite 1	Metabolite 2	Metabolite 3
logPow	≤ 0.2	- 0.2	Not relevant	Not relevant
Bioconcentration factor (BCF)1 ‡	Not relevant	Not relevant		
Annex VI Trigger for the bioconcentration factor				
Clearance time (days) (CT50)				
(CT90)				
Level and nature of residues (%) in organisms after the 14 day depuration phase				

[1] only required if log $P_{O/W}$ > 3.
* based on total ^{14}C or on specific compounds

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)
Sulcotrione ‡	50 µg as/bee	200 µg as/bee
Preparation1	763 µg formulation/bee	763 µg formulation/bee
Metabolite		
Field or semi-field tests: not required		

[1] For preparations indicate whether endpoint is expressed in units of as or preparation

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

Crop and application rate

Test substance	Route	Hazard quotient	Annex VI Trigger
Sulcotrione	Contact	2.3	50
Sulcotrione	oral	9	50
Preparation	Contact	2.2	50
Preparation	oral	2.2	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	Endpoint	Effect (LR_{50} g/ha[1])
Typhlodromus pyri ‡	Sulcotrione SC300	Mortality	> 450 g as/ha
Aphidius rhopalosiphi ‡	Sulcotrione SC300	Mortality	> 450 g as/ha

[1] For preparations indicate whether endpoint is expressed in units of as or preparation

Maize, 450 g as/ha post emergence

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
Sulcotrione SC300	*Typhlodromus pyri*	> 450 g as/ha	< 1	0.055 (VDF 5)	2
Sulcotrione SC300	*Typhlodromus pyri*	> 450 g as/ha	< 1	< 0.0277 (VDF 10)	2
Sulcotrione SC300	*Aphidius rhopalosiphi*	> 450 g as/ha	< 1	< 0.055 (VDF 5)	2
Sulcotrione SC300	*Aphidius rhopalosiphi*	> 450 g as/ha	< 1	< 0.0277 (VDF 10)	2

0 indicate distance assumed to calculate the drift rate

Test substance	Species	Effect (LR50 g/ha)	TER off-field1	Trigger value
Sulcotrione SC300	*Typhlodromus pyri*	> 450 g as/ha	> 181 (1 m)	10
Sulcotrione SC300	*Aphidius rhopalosiphi*	> 450 g as/ha	> 181 (1 m)	10
Sulcotrione SC300	*Pardosa spp.*	10.34 g as/ha	4 (1 m) 20 (5 m)	5

[1] TER approach used by the German Federal Environmental Agency (Schulte et al., 1999: UWSF 11(5) 261-266).
PEC off-crop = Single application rate × drift factor/VDF(5). Without VDF if product is sprayed on plants.

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)[1,2]	Endpoint	% effect[3]	Trigger value
Coccinella septempunctata	larvae	Sulcotrione SC300; glass plates; 19 d (+ reproduction)	1, 4, 15, 50, 180 g as/ha; initial residues	mortality	LR50 = 5.7 g as/ha	50 %
Aphidius rhophalosiphi	adults	Sulcotrione SC300; maize leaves, 2 D, 48 h (+ 11 d)	12, 5; 450 g as/ha	mortality effect on reproduction	0 % 41.8 %	50 %
Poecilus cupreus	adults	laboratory, spray application on quartz sand, 14 d	450 g as/ha	mortality effect on feeding rate	0 % 0 %	50 %
Aleochara bilineata	adults	laboratory, spray application on sand, 4w (+hatching period); duration 11w	450 g as/ha	effect on reproduction	35.3 %	50 %
Aleochara bilineata	adults	extended laboratory, spray application on loamy soil, 61d	450 g as/ha	corrected mortality effect on parasitation rate	0 % 3.6 %	50 %
Pardosa spp.	adults	laboratory, spray application on quartz sand, 14 d	440 g as/ha	corrected mortality effect on feeding rate	58.8 % 41.2 %	50 %
Pardosa spp.	adults	extended laboratory, spray application on standard soil, 21d	440 g as/ha	corrected mortality effect on feeding rate	96.8 % 41.2 %	50 %

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)[1,2]	Endpoint	% effect[3]	Trigger value
Pardosa spp.	adults	extended laboratory, spray application on standard soil, 21d;	4, 10, 24.6, 60.7, 150 g as/ha	LR_{50} 10 g as/ha corrected mortality effect on feeding rate	10.34 g as/ha 46.8 % 14.4 %	50 %
Pardosa spp.	adults	extended laboratory, spray application on standard soil (LUFA 2.1), 21d;	450 g as/ha	fresh residues: corrected mortality effect on feeding rate residues aged for 14 days corrected mortality: effect on feeding rate residues aged for 28 days corrected mortality effect on feeding rate residues aged for 42 days corrected mortality effect on feeding rate	88.2 % 45.4 % 28.2 % 21.0 % 29.9 % 26.1 % 30.4 % 18.6 %	50 %

[1] indicate whether initial or aged residues
[2] for preparations indicate whether dose is expressed in units of as or preparation
[3] indicate if positive percentages relate to adverse effects or not

Field or semi-field tests
No data submitted. Data required if risk mitigation measures will not be accepted (5 m buffer zone)

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	Endpoint[1]
Earthworms			
Eisenia foetida	Sulcotrione ‡	Acute 14 days	LC_{50} > 1000 mg as/kg dw soil
	Sulcotrione	Chronic 8 weeks	Not relevant
Eisenia foetida	Preparation (300 SC)	Acute 14 days	LC_{50} > 1000 mg as/kg dw soil
	Preparation	Chronic	Not relevant
Eisenia foetida	Metabolite CMBA	Acute 14 days	LC_{50} > 1000 mg as/kg dw soil
	Metabolite	Chronic	Not relevant
Other soil macro-organisms			
Soil mite	Sulcotrione		Not relevant
	Preparation		Not relevant
	Metabolite		Not relevant
Collembola			
	Sulcotrione	Chronic	Not relevant
	Preparation	Chronic	Not relevant
	Metabolite CMBA	Chronic	NOEC 32 mg as/kg dw soil
	Metabolite	Chronic	Not relevant
Soil micro-organisms			
Nitrogen mineralisation	Sulcotrione	28 d	both soils 0.45 kg as/ha 4.5 kg as/ha
	Metabolite	28 d	both soils 0.2 mg/kg < 25 % reduction 1.0 mg/kg < 25 % reduction
Carbon mineralisation	Sulcotrione	27 d	both soils: 0.45 kg as/ha 4.5 kg as/ha
	Metabolite	28 d	both soils 0.2 mg/kg < 25 % reduction 1.0 mg/kg < 25 % reduction
Field studies2			
Not relevant			

[1] indicate where endpoint has been corrected due to log $P_{o/w}$ > 2.0 (e.g. LC_{50corr})
[2] litter bag, field arthropod studies not included at 8.3.2/10.5 above and earthworm field studies

Toxicity/exposure ratios for soil organisms

Crop and application rate

Test organism	Test substance	Time scale	Soil PEC[2]	TER	Trigger
Earthworms					
Eisenia foetida	Sulcotrione ‡	Acute	0.4500 mg/kg (PECi)	> 2222	10
	Sulcotrione	Chronic		Not relevant	5
Eisenia foetida	Preparation (300 SC)	Acute	0.4500 mg/kg (PECi)	> 2222	10
	Preparation	Chronic		Not relevant	5
Eisenia foetida	Metabolite CMBA	Acute	0.1574 mg/kg (PECi)	> 6353	10
	Metabolite	Chronic		Not relevant	5
Other soil macro-organisms					
Soil mite	Sulcotrione			Not relevant	
	Preparation			Not relevant	
	Metabolite			Not relevant	
Collembola	Sulcotrione	Chronic		Not relevant	
	Preparation	Chronic		Not relevant	
	Metabolite CMBA	Chronic	0.1092 mg/kg (PECi)	293	5
	Metabolite	Chronic		Not relevant	

[1] to be completed where first Tier triggers are breached
[2] indicate which PEC soil was used (e.g. plateau PEC)

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

Preliminary screening data

Not required for herbicides as ER_{50} tests should be provided.

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g/ha)[2] vegetative vigour	ER_{50} (g/ha)[2] emergence	Exposure[1] (g/ha)[2]	TER	Trigger
Lactuca sativa	Preparation (300 SC)		7	PEC 6.23 (as) 1 m buffer	1.1	5
Lactuca sativa	Preparation (300 SC)		7	PEC 1.28 (as) 5 m buffer	5.5	5
All tested species	Preparation (300 SC)	HC5 2.58 (as)		PEC 12.47 (as) 1 m buffer	0.2	≥ 2
All tested species	Preparation (300 SC)	HC5 2.58 (as)		PEC 2.57 (as) 5 m buffer and 50 % drift reducing nozzles or 10 m buffer	2	≥ 2
Brassica rapa	Metabolite CMBA		30000	PECi 118 (as)	Not relevant	
All tested species	Metabolite CMBA	> 4480			Not relevant	

[1] explanation of how exposure has been estimated should be provided (e.g. based on Ganzelmeier drift data)
[2] for preparations indicate whether dose is expressed in units of as or preparation

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

Not relevant

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

Test type/organism	endpoint		
Activated sludge	Sulcotrione:	EC_{50} [mg as/L]	4060
	Metabolite (CMBA):	EC_{50} [mg as/L]	60
Pseudomonas sp.	Sulcotrione:	EC_{50} [mg/L]	> 180
	Metabolite (CMBA):	EC_{50} [mg as/L]	> 100

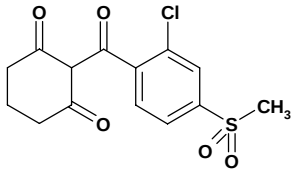
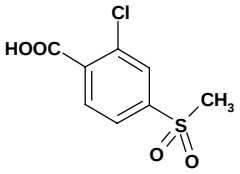
Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Compartment	
soil	Parent (Sulcotrione)
water	Parent (Sulcotrione)
sediment	Parent (Sulcotrione)
groundwater	Parent (Sulcotrione)

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

	RMS/peer review proposal
Active substance	N, R50/R53 dangerous to the environment very toxic to aquatic organisms, may cause long-term effects (based on *Lemna* E_rC_{50} 0.072 mg as/L)

	RMS/peer review proposal
Preparation	Not included

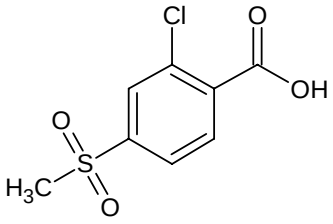
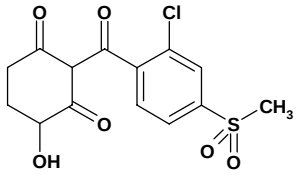
Code/Trivial name	Chemical name	Structural formula
Sulcotrione	2-[2-chloro-4-methylsulfonyl)benzoyl]-1,3-cyclohexanedione (IUPAC)	
CMBA	2-chloro-4-(methylsulfonyl)-benzoic acid (IUPAC)	

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
CMBA (M01)	2-chloro-4-(methylsulfonyl)-benzoic acid	
M02	2-[2-chloro-4-(methylsulfonyl)benzoyl]-4-hydroxycyclohexane-1,3-dione (IUPAC) 4-hydroxy-sulcotrione	
M04	2-[2-chloro-4-(methylsulfonyl)benzoyl]-5-hydroxycyclohexane-1,3-dione (IUPAC) 5-hydroxy-sulcotrione