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

cadusafos

finalised: 24 April 2006

SUMMARY

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

Greece being the designated rapporteur Member State submitted the DAR on cadusafos in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 1 June 2004. Following a quality check on the DAR, the peer review was initiated on 4 August 2004 by dispatching the DAR for consultation of the Member States and the sole applicant FMC Chemical. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting on 9 February 2005. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in June and July 2005.

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

The conclusion was reached on the basis of the evaluation of the representative as insecticide and nematicide comprise the application by spraying or via the drip irrigation system to control a range of soil insects and nematodes in bananas and potatoes at application rates of up to 6 kg cadusafos per hectare. In case of potatoes incorporation into soil takes place after the application. Cadusafos can be used as insecticide and nematicide. It should be noted that during the peer review process the applicant stated that only the use in bananas will be supported in the EU review process.
The representative formulated product for the evaluation was "Ruby 200 CS", a capsule suspension (CS). Preparations containing cadusafos are registered in Cyprus, France, Greece and Spain.

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

Adequate methods are available to monitor all compounds given in the respective residue definition only for soil, water and air, i.e. cadusafos in soil, water and air.
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.
Insufficient data are available for the determination of cadusafos in the technical material and in the representative formulation to ensure that quality control measurements of the plant protection product are possible.

The absorption of cadusafos is extensive and rapid, the excretion is mainly via urine, without evidence of body accumulation. The acute oral toxicity is high, and the acute inhalation and dermal toxicity are very high. The proposed classification is T^+, R26/27 "Very toxic by inhalation and in contact with skin"; T, R25 "Toxic if swallowed".
The main effect after short term oral administration is the decrease of cholinesterase activities in all species. Cadusafos has no genotoxic potential and is not considered to be carcinogenic. In the two-generation rat study, there was no effect on reproductive performance or fertility, and in the rat and rabbit teratology studies, no evidence of teratogenic effects in the absence of maternal toxicity.
Supplementary studies were performed due to the introduction of a new impurity in the technical material. The acute and subchronic oral tests revealed no difference in toxicity. The Ames test was negative.
The Acceptable Daily Intake (ADI) is 0.0004 mg/kg bw/day, the Acceptable Operator Exposure Level (AOEL) is 0.0007 mg/kg bw/day, and the Acute Reference Dose (ARfD) is 0.003 mg/kg bw/day. The comparison of the oral and dermal LD_{50} values results in a dermal absorption value of 100%. The operator exposure estimates are based solely on one specific and restricted representative use in bananas, with automatic drip irrigation, work rate of 1 ha/day, application rate of 6 kg a.s./ha, and assuming that the microcapsules in the formulation do not release cadusafos until they are diluted for application. The results are below the AOEL according to the currently used models which do not apply properly to this particular scenario. Worker and bystander exposures are expected to be very low due to the mode of application by drip irrigation.

The metabolism of cadusafos has been investigated on several crops after soil application.
The representative use on potatoes can be considered as adequately covered by these data and the residue definition for this use can be cadusafos only, for both monitoring and risk assessment. The available residue trials in potatoes for Southern Europe are however not sufficient to draw a robust conclusion on the residue levels consumers may be exposed to. The available data suggest that residues are below 0.01 mg/kg, but results from trials in Northern Europe indicate that the currently available data may underestimate the actual situation. Further supervised residue trials should be carried out.
For the representative use on bananas, although 2 metabolism studies for this crop were submitted, the data are not sufficient to propose a residue definition. This is due to major deficiencies in the studies, making it impossible to evaluate the possible presence of degradation products still exhibiting the anticholinesterase activity of the parent compound. Therefore a new metabolism study in bananas

is needed as well as residue trials carried out according to the representative use pattern. The compounds to be analysed in the residue trials should be determined on the basis of the results of the metabolism study.
The situation for rotational crops has not been addressed by the notifier, although the soil persistence of the compound exceeds the trigger value for conducting uptake and metabolism studies in succeeding crops. Therefore these studies should be requested.
Based on the current knowledge of the residue situation in potatoes, the exposure of livestock is very low and metabolism studies in domestic animals do not need to be carried out.
Only preliminary acute and chronic exposure assessments could be conducted for the use on potatoes, but these assessments need to be re-examined on the basis of complete and robust data. No MRLs can be proposed at this stage.

The available data demonstrate that in soil cadusafos degrades to the minor (<10% applied radioactivity (AR)) metabolite methyl-2-butyl sulfone. Mineralisation of the butyl-2-^{14}C radiolabel accounted for 43-71%AR after 90-120 days incubation at 25°C. The values for residues not extracted by acetonitrile / water were 25-32% AR after 90-120 days. In soil cadusafos exhibited moderate persistence and methyl-2-butyl sulfone exhibited low persistence.

In guideline batch soil adsorption studies cadusafos exhibited medium mobility. There was no evidence of pH dependant adsorption. Data on the adsorption of methyl-2-butyl sulfone were not available. As this metabolite accounted for > 5%AR at 2 consecutive sampling points in a soil route of degradation study, information on its mobility in soil is required to complete the groundwater exposure assessment for this metabolite.

In sediment water systems cadusafos exhibited moderate persistence and produced no major metabolites. It dissipated by partitioning to sediment, volatilising and mineralising to CO_2 (butyl-2-^{14}C radiolabel accounted for 12-18%AR after 100 days incubation at 20°C). Residues not extracted from sediment by acetonitrile/water accounted for only 6-8%AR at 100 days.

The available aquatic exposure assessment from the use on bananas (application via drip irrigation) just in Tenerife indicated that surface water exposure and consequently sediment exposure would be negligible. This conclusion is specific to this use in Tenerife and should not be applied to bananas grown elsewhere. The available aquatic exposure assessment from the use on potatoes is appropriate for addressing the spray drift route of entry to surface water for initial PEC in aquatic systems. However MS would need to carry out a surface water exposure and consequent aquatic risk assessments from the runoff and drainage routes of exposure at the national level, as the available EU level assessment does not cover these situations.

The available FOCUS groundwater modelling for potatoes and the specifically parameterised scenario for bananas in Tenerife for parent cadusafos has not been carried out with appropriate soil DT_{50} or Henry's law parameters. The potential for groundwater contamination is therefore currently

unclear. New groundwater modelling is therefore required for cadusafos. A groundwater leaching assessment for the soil metabolite methyl-2-butyl sulfone is triggered. It is not available.

Cadusafos is moderately volatile and volatilisation will contribute to dissipation from soil and water. However cadusafos is not expected to be subject to long range transport via the upper atmosphere due to a relatively rapid calculated photochemical oxidative degradation rate with hydroxyl radicals.

In the first tier assessment an acute and long-term risk was identified for insectivorous birds. A risk was also identified for earthworm-eating birds and mammals as well as for fish-eating birds and mammals for the use in potatoes. Since the use in potatoes was withdrawn by the applicant the refinements of the risk to birds and mammals from this use was not further considered. For the use in banana plantations a conclusion on the risk to birds and mammals can not be reached at this stage. The risk needs to be further addressed based on species that occur in banana plantations and their associated diets.

Cadusafos is very toxic to fish and aquatic invertebrates. The assessment indicates a high risk. However, for the specific use in banana plantations in Tenerife the risk to aquatic organisms is considered low based on negligible contamination of surface water.

The toxicity to bees is high, but since for the proposed uses application will be to bare soil the risk is considered low. No in-field exposure of leaf dwelling non-target arthropods is expected from the evaluated uses. The available test with *Poecilius cupreus* was conducted at an application rate which is lower than the proposed. An ongoing study with *Aleochara bilineata* should be submitted for the use in banana due to the perceived low sensitivity of *P. cupreus*. For the application of cadusafos by drip-irrigation to banana plants no off-field exposure is expected.

A high acute and long-term risk was identified for earthworms. The ongoing field study conducted in United Kingdom should be submitted and the relevance for the proposed uses should be addressed. It should be noted that the application rate in this study is 4.5 kg cadusafos per hectare, which is below the proposed application rate for the intended uses. A study with Collembola and mites is required to address the risk to other soil macro-organisms. The risk to soil micro-organisms and biological methods of sewage treatment plants is low. For the drip irrigation use in banana no off-crop exposure is expected and hence the risk to non-target plants is considered low.

Key words: cadusafos, peer review, risk assessment, pesticide, insecticide, nematicide

TABLE OF CONTENTS

BACKGROUND

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

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, Greece submitted the report of its initial evaluation of the dossier on cadusafos, hereafter referred to as the draft assessment report, to the EFSA on 1 June 2004. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the revised version of the draft assessment report was distributed for consultation on 4 August 2004 to the Member States and the sole applicant FMC Chemical.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed in an evaluation meeting on 9 February 2005 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier attended this meeting.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised on behalf of the EFSA by the EPCO-Team of the Pesticide Safety Directorate (PSD) in York, United Kingdom in June and July 2005. The reports of these meetings have been made available to the Member States electronically.

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

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

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

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

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

- the comments received
- the resulting reporting table (rev. 1-1 of 9 March 2005)
- 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 6 March 2006)

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

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Cadusafos is the ISO common name for *S,S*-di-*sec*-butyl *O*-ethyl phosphorodithioate (IUPAC).

Cadusafos belongs to the class of aliphatic organothiophosphate insecticides such as ethoprophos and malathion and to the class of organothiophosphate nematicides such as dimethoate and ethoprophos. Cadusafos acts by contact and ingestion (systemic action) and inhibits the enzyme acetylcholinesterase.

The representative formulated product for the evaluation was "Ruby 200 CS", an capsule suspension (CS). Preparations containing cadusafos are registered Cyprus, France, Greece and Spain.

The evaluated representative uses as insecticide and nematicide comprise the application by spraying or via the drip irrigation system to control a range of soil insects and nematodes in bananas and potatoes at application rates of up to 6 kg cadusafos per hectare. In case of potatoes incorporation into soil takes place after the application. Cadusafos can be used as insecticide and nematicide. It should be noted that during the peer review process the applicant stated that only the use in bananas will be supported in the EU review process.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of cadusafos as manufactured should not be less than 900 g/kg. However, this value and the values for the maximum content of the impurities in the technical material must be regarded as provisional due to the outstanding new 5-batch analysis. Furthermore, additional information on the content of one impurity is required to ensure that the current proposed maximum value is covered.
For the moment no FAO specification exists.

The technical material contains no relevant impurities.

The content of cadusafos in the representative formulation is 200 g/L (pure).

Beside the provisional 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 cadusafos or the respective formulation. However, the following data gaps were identified:

- a study for the determination of the surface tension of the preparation,
- clarification with respect to the viscosity (shear rate) of the preparation,
- data on the suspensibility and spontaneity of dispersion after freeze/thaw cycles of the preparation, and
- data on the effectiveness of the cleaning procedure.

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

The assessment of the data package revealed the following data gaps with respect to the analytical methods:

- validation data for the analytical methods used for the determination of cadusafos as well as for certain impurities in the technical material and cadusafos in the formulation.
- an ILV for the analytical methods used for the determination of cadusafos in bananas and potatoes, and
- a confirmatory method for the determination of residues of cadusafos in blood as well as an analytical method for animal tissues (meat or liver).

Therefore, insufficient data are available for the determination of cadusafos in the technical material and in the representative formulation to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor all compounds given in the respective residue definition only for soil, water and air, i.e. cadusafos in soil, water and air.
Methods are available for the determination of cadusafos in food of plant origin (bananas and potatoes), but the applicability of the method for the determination of residue in food of plant origin depends on the final residue definitions (see. 3.4 and 6). It should be noted that if cadusafos is the relevant residue in bananas, the applicability of the method has to be confirmed by the outstanding independent laboratory validation (ILV) as it is required for potatoes.
A validated analytical method for the determination of cadusafos in blood is available but confirmatory method in blood and a validated analytical method for animal tissues (meat or liver) are required to address Annex point 4.2.5 of Directive 96/46/EC.
The methodology used is GC with PN, FP or MS detection. A multi-residue method like the Dutch MM1 or the German S19 is not applicable to due the nature of the residues.
An analytical method for food of animal origin is not required due to the fact that no MRLs are proposed (see 3.4).

The discussion in the expert meeting (EPCO 30, July 2005) on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material, some physical, chemical and technical properties of the preparation and the analytical methods.

2. Mammalian toxicology

Cadusafos was discussed at EPCO experts' meeting for mammalian toxicology (EPCO 28) in June 2005.

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

Cadusafos is rapidly and extensively absorbed after oral administration in rats (approximately 80% within 168 hours), and excreted mainly via urine (70% within 24 hours), secondarily via the expired air (up to 17%). There is no evidence of accumulation, the highest concentrations are observed in liver, fat, kidneys and lungs. The metabolic pathway of cadusafos in rats is extensive and includes cleavage of the thio-(sec-butyl) or O-ethyl- groups, oxidation and methylation.

2.2. Acute toxicity

Cadusafos is of high acute oral toxicity and of very high acute inhalation and dermal toxicity, based on the respective studies in rats (oral LD_{50} 30.1 mg/kg bw, inhalative LC_{50} 0.026 mg/L), mice (oral LD_{50} 68 mg/kg bw), and rabbits (dermal LD_{50} 10.7 mg/kg bw). Cadusafos is not classified irritant to the skin and is not a skin sensitizer. The experts noted that the eye irritation study was not completed due to mortality (observations at 1 hour showed only a slight eye irritation), and thus it is not possible to classify cadusafos with respect to eye irritation.
Based on the above mentioned results, **the following classification is proposed: T^+, R26/27 "Very toxic by inhalation and in contact with skin"; T, R25 "Toxic if swallowed".**

2.3. SHORT TERM TOXICITY

The target effect in short term studies is the decrease of acetyl cholinesterase (AChE) activities in all species (rats, mice and dogs) after oral administration.

The relevant NOAEL is 0.067 mg/kg bw/day, from the 90-day rat study, based on inhibition of erythrocyte AChE and changes in kidney weight.

There is no short term inhalation study with cadusafos, whereas it is very toxic by inhalation and its volatility is above the vapour pressure that triggers a requirement for toxicity data after repeat exposure by inhalation. Even if the supported use is an encapsulated formulation, the experts agreed to set a **new data requirement** and the notifier is asked to address **potential short term inhalation toxicity**.

2.4. GENOTOXICITY

The genotoxic potential of cadusafos was investigated in a battery of *in vitro* and *in vivo* mutagenicity assays.

Results *in vitro* show that cadusafos does not induce forward mutations or chromosome aberrations in CHO cells, DNA repair in rat hepatocytes, but induces an increase in the incidence of focus formation in the morphological transformation assay in mouse embryo cells (in the presence of metabolic activation). *In vivo*, cadusafos does not induce any significant increase of chromosome aberrations in rat bone marrow cells.

From the overall evaluation of the in *vitro* and *in vivo* genotoxicity studies, it was concluded that cadusafos has no genotoxic potential.

2.5. LONG TERM TOXICITY

In oncogenicity/chronic toxicity studies in rats and mice, plasma and erythrocyte AChE activities are consistently depressed, while no effect on brain AChE is observed. In the rat study, the NOAEL is 0.045 and 0.056 mg/kg bw/day for males and females, based on RBC AChE inhibition and decreased locomotion.

In the mouse study, the NOAEL is 0.072 mg/kg bw/day in males, based on renal necrotizing arteritis, and 0.189 mg/kg bw/day in females, based on RBC AChE inhibition, adrenal cortical atrophy and duodenum avillous mucosal hyperplasia.

The tumour formation observed in male mice (lymphoreticular neoplasms, lung combined bronchiolar-alveolar adenocarcinoma and adenoma, liver combined adenocarcinomas and adenomas) is not considered to be directly related to cadusafos treatment since it is not statistically significant, or not dose-related. Cadusafos is not considered to be carcinogenic.

2.6. REPRODUCTIVE TOXICITY

One two-generation and one teratogenicity studies have been performed with rats, and one teratogenicity study with rabbits.

In the two-generation rat study, cadusafos has no effect on reproductive performance of fertility. The NOAEL for the offspring and the reproductive NOAEL are 0.371 mg/kg bw/day, and the parental NOAELs is 0.026 (males) and 0.030 (females) mg/kg bw/day based on decreased body weight and AChE activities (plasma and erythrocyte).

In the rat teratology study, severe maternal effects are observed at the high dose (decreased weight gain and clinical signs) as well as developmental effects (decreased foetal body weight and delayed skeletal ossification, including absence of the xiphoid bone). Absence of the xiphoid bone is also noted at the mid dose (6 mg/kg bw/day) not associated with cholinergic clinical signs in 6 dams (only in 2 dams). As no AChE measurement is available, the experts have taken into account the previous results of subchronic and chronic studies with rats and have agreed that significant AChE inhibition was likely to occur in the dams at this dose. It was also considered that assessment of the xiphoid bone was technically difficult and that historical incidence of this skeletal variation is no longer recorded. Finally it was concluded that in the absence of any other skeletal finding, this was not an adverse effect. However, the classification of cadusafos for developmental effects will be discussed at the next ECB Classification and Labelling Meeting (March 2006).

In the rabbit teratology study, there was no evidence of teratogenicity in the absence of substantial maternal toxicity. The relevant maternal and developmental NOAELs, from the rabbit study, are 0.3 mg/kg bw/day, based on clinical signs of cholinergic toxicity and decreased number of live fetuses due to an increased number of early resorptions.

2.7. NEUROTOXICITY

The neurotoxic potential of cadusafos is evaluated in the DAR by a single acute study in hens which gave no evidence of delayed neurotopathy and a NOAEL of 8.0 mg/kg bw/day. However, this study is considered as indicative due to major deviations.

Two new studies are presented in an addendum: an acute and a subchronic neurotoxicity study in rats. Clinical signs and decrease in AChE activities are observed, and the resulting NOAEL is 0.03 mg/kg bw/day. The experts noted that the large dose spacing hindered the derivation of reference doses from these neurotoxicity studies.

2.8. FURTHER STUDIES

Plant metabolites

No toxicity studies on metabolites were submitted by the notifier.

The relevance of two major non rat metabolites of cadusafos, M2 (1-carboxy-hydroxyisopropylmethylsulfone) and its isomer M3 (both found in potato tubers) is discussed in the DAR. These two metabolites are considered to be less toxic than the parent compound due to their high polarity characteristics (e.g chemical structure, absence of the OP-toxophor) and to their derivation from a common plant and rat metabolite (hydroxy-2-butylmethylsulfone). Furthermore, it is stated the M2 and M3 are transient metabolites, which are likely to be biotransformed *via* decarboxylation to carbon dioxide.

Conclusively, the metabolites M2 and M3 are considered of no toxicological concern.

Hydroxy-2-butane sulfonic acid is not a rat metabolite, and no toxicity studies were submitted by the notifier (it is found in banana pulp). The experts noted that it does not contain the OP part of cadusafos, that sulfonic acids are of relatively low toxicity, and that as a result it was postulated to be of lower toxicity than the parent. It was concluded that the notifier should be requested to submit a position paper on the toxicity of hydroxy-2-butane sulfonic acid.

Impurities

As a consequence of a change in the manufacturing process for cadusafos and the introduction of a new impurity, several supplementary studies were conducted in order to ascertain the toxicological equivalence of the old and the new technical. The oral acute study in rats and oral 90-day study in dogs revealed no significant difference. The first Ames test gave negative results but was considered invalid by the RMS due to lower titres of viable bacterias in two strains, than those set by the protocol criteria. In a new Ames test, no genotoxic effects were observed but the level of impurity could not be confirmed in the batch used. Thus a data requirement was set for further batch analysis. A position paper has been submitted by the notifier after the expert meeting but not evaluated.

2.9. MEDICAL DATA

Only an AChE monitoring was performed in two production plants, and to date, there have been no issues with depressed AChE levels.

On the other hand, the experts agreed that, based on the toxicological properties of cadusafos, reports of poisoning incidents could be available. Thus a data requirement was set during the meeting.

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

The initial proposals of reference values were derived with the use of a safety factor of 300 due to insufficient neurotoxicity data in the DAR (additional safety factor of 3). With the results of the new neurotoxicity studies, reported in an addendum, the experts agreed to reduce the safety factor to 100.

ADI

The ADI is 0.0004 mg/kg bw/day, based on the 2-year rat study.

AOEL

The AOEL is 0.0007 mg/kg bw/day, based on the 90-day rat study.

ARfD

The first proposal of ARfD was based on the 28-day rat study. The experts agreed to use the rabbit developmental toxicity study instead, where the increase in early resorptions with no increase in late resorptions was considered consistent with the time at which administration of cadusafos starts. Thus, the ARfD is 0.003 mg/kg bw/day.

2.11. DERMAL ABSORPTION

No studies were submitted. The approach agreed by the MS is based on the comparison of the acute oral and dermal LD_{50} values, resulting in a dermal absorption value of 100% of cadusafos technical.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Rugby 200 CS is a capsule suspension containing 200 g cadusafos/L for application on soil. In the DAR, the supported crops were potatoes and bananas but during the peer-review, the supported uses were limited to treatment of bananas by drip irrigation.

Operator exposure

According to the intended uses submitted by the applicant the maximum applied dose is 6 kg cadusafos/ha and the minimum volume of water is 20,000 L/ha. The only supported use is treatment of bananas by drip irrigation.

Operator exposure calculations concern only the mixing/loading process where no pouring operations are required but a direct injection system is used. According to the notifier, the typical size of a banana plantation in the Canary Islands is 1 ha, and the drip irrigation process takes between 2 and 4 hours. An operator is not expected to treat more than one plantation per day.

The release of cadusafos from microcapsules (Rugby 200CS) after dilution in water has been studied and the results show that 1.12% of the total amount is bioavailable (free) after 2 minutes (and 4.10% after 4 hours). This value is used as a worst case for "free" cadusafos in the concentrate. Nevertheless, no information on the stability of the microcapsules during storage is available.

The estimated operator exposure during mixing and loading is below the AOEL with PPE, according to the German and UK POEM models (tractor-mounted boom sprayer, work rate 1ha/day, operator body weight 60 kg), see table beneath.

Estimated exposure presented as % of AOEL (0.0007 mg/kg bw/day), according to calculations with the German and UK POEM model. The default for body weight of operator is 60 kg in both models.

Model	No PPE	With PPE:
German	352	11
UK POEM (5L container)	334	17
UK POEM (20L container)	559	28

PPE (personal protective equipment): gloves during mixing/loading

EFSA notes: The standard models used to assess operator exposure are not directly applicable to the scenario under consideration. Furthermore, a lot of assumptions and/or restrictions have been applied to the assessment :

- automatic drip irrigation (no hand held application considered)

- use of gloves during mixing/loading
- work rate of 1 ha/day (very particular input not applicable on a standard basis)
- no release of "free" cadusafos from the microcapsules above 1.12% (this is not fully reliable due to a lack of information on the stability of the microcapsules before dilution)

Worker exposure

No data has been submitted by the notifier. In case of accidental exposure of workers to irrigation solution, it is expected to be very low taking into consideration that:

- the solution is highly diluted (in 20,000 to 50,000 L of water)
- a maximum of 4.1% of the total cadusafos contained in the product has been released in aqueous solution after 4 hours while the irrigation process lasts between 2 to 4 hours.

No further consideration of worker exposure was considered necessary by the experts.

Bystander exposure

As the application is only to bananas by drip irrigation, there is no chance for exposure outside of the target zone. No assessment of the bystander's risk was considered necessary by the experts.

EFSA notes: Since there is no information about the stability of the microcapsules during storage and the fact that cadusafos is volatile, the exposure to airborne residues might be possible.

3. Residues

Cadusafos was discussed at an EPCO experts' meeting for residues (EPCO 29) in July 2005.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism and translocation of cadusafos[3] were investigated in maize (2 kg a.s./ha) banana (2 studies, 3 g a.s./tree, 0.75N) radish (9 kg a.s./ha) and potato (6 kg a.s./ha, N). In accordance with the applied for intended uses the substance was applied as soil treatment. Radish and potatoes were planted in the soil immediately after treatment, maize immediately before treatment. In the banana experiments the soil was treated when mature trees were at the early fruiting growth stage. The intervals between soil application and the sampling of plant parts were: 30-106 days for maize, 50 days for radish, 90-158 days for banana and 160 days for potatoes.

The metabolism studies on bananas were extensively discussed during the expert meeting (EPCO 29) for their reliability and relevance for the supported representative use. A major deficiency identified by the experts was the too long delay in the studies between application and harvest of samples in comparison to the proposed PHI (14 days as proposed by the notifier, or 28 days as alternatively

[3] Note in addition to the information in the DAR additional argumentation/clarification was included in the addendum to the DAR dated June 2005.

proposed by the RMS). Information is therefore only available for long PHIs, with hydroxy-2-butane sulfonic acid, methyl-2-butyl sulfone and 3-hydroxy-methyl-2-butyl sulfone being the main organosoluble degradation products identified in bananas. Unchanged cadusafos was also present in low amounts. No information is available on the residue pattern for short delays after application. In addition to that, an important discrepancy in the levels of residue uptake was observed between the two studies, probably related to different conditions of soil and/or climate, but not explained by the notifier. The expert concluded that the information on the nature of residues potentially present in bananas from a PHI of 14 days was not provided and that a new study should be conducted, investigating several PHIs to give a clear picture of the evolution of the residue pattern along time and to allow a safe decision on the residue definition. In particular the presence of 2 metabolites observed in maize plants at short PHIs and still containing the phosphorothiate moiety (S,S-di(2-butyl)-phosphorothioic acid and S-(2-butyl)-phosphorothioic acid) and therefore potentially having cholinesterase inhibition activity, should be carefully investigated.

It was concluded that the available potato metabolism study was of an acceptable design, and was appropriate to support the applied for intended use on potato. Low amounts of cadusafos (about 1% of the Total Radioactive Residues) were present at harvest in mature tubers. One major metabolite consisting in the 2 isomers of 1-carboxy-hydroxyisopropylmethylsulfone and present as conjugate was identified. This metabolite is not expected to be a cholinesterase inhibitor on the basis of its chemical structure as mentioned under point 2.8. Therefore, the appropriate residue definition applicable to potatoes for both monitoring and risk assessment should be parent cadusafos only.

The currently available supervised residue trials have analysed for residues of parent cadusafos only. For potatoes, 4 acceptable residue trials reflecting the applied for intended use are available from Southern Europe. In these studies, residues were always below 0.01 mg/kg, being the LOQ (Limit Of Quantification) used in these trials. These results must however be carefully considered because residue trials carried out in the North for the purpose of processing studies demonstrated the presence of residues ranging from 0.02 to 0.05 mg/kg for similar application rates. The metabolism study on potatoes gives similar indication. A data gap was therefore identified for a further 4 trials in southern Europe to be completed. Member State experts considered a validated limit of analytical quantification of 0.005 mg/kg would need to be achieved for these additional trials. Achieving this low analytical limit of quantification is important because of the low mammalian toxicology reference endpoints that have been derived (see section 2.10). The data gap for 4 additional residue trials in potatoes is not supported by the RMS, which considers that the provided information is sufficient to prove that the use of cadusafos in Southern Europe leads to a no-residue situation.

For bananas no residues trials reflecting the applied for intended southern EU use are available from southern Europe. A data gap was therefore identified. Further residues trials on bananas to fill this identified data gap would need to take into account the results of the required plant metabolism study on bananas that has also been identified as a data gap.

Storage stability studies were provided, demonstrating that cadusafos is stable under deep freeze conditions (-18 °C) for at least 15 months.

Given the low level of cadusafos residues in raw commodities, no study was carried out for investigating the effect of processing on the nature of the residues. The notifier has however provided

for informative purpose 3 studies on the effect of processing on the residue levels in processed potatoes. These studies suggest that residues are mainly located on the peel of the potatoes.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Parent cadusafos has a single first order field DT_{90} in soil under southern European conditions of up to 206 days (see section 4.1.2). Therefore for crops grown in rotation such as potatoes, information on potential residue in following crops is required (the time from treatment pre-planting to harvest will be around 160 days). This soil DT_{90} only relates to the parent active ingredient. In addition to the potential for uptake from soil of parent cadusafos, the potential for soil degradation products to be taken up by crops grown in rotation after the treated crop also needs to be addressed. No experimental data are available in the dossier to address the potential for residues present in soil to be taken up by a range of potential succeeding crops. Therefore it is clear that there is a data gap for the potential for residues in following crops to be addressed in relation to the applied for intended use on potatoes.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Based on the residue levels from the incomplete residues trials data set on potatoes available at the time this conclusion was finalised, when EU guidance is followed, an assessment of residues in products of animal origin is not required. (As theoretical maximum daily intakes by domestic animals from the consumption of potatoes does not exceed 0.1 mg/kg diet). However this low intake estimate would need to be checked should the results from the residues trials on potato identified as a data gap become available. Bananas are not considered to be a significant constituent of the diets of domestic animals in the EU.

3.3. CONSUMER RISK ASSESSMENT

A consumer risk assessment is difficult to be conducted at this stage given the lack of relevant information for banana and the incomplete residues trials data set available on potatoes and bananas.
However, preliminary chronic and acute exposure assessments based on the 4 available residue trials on potatoes were carried out by the RMS.
As far as chronic exposure is concerned, considering a residue level in potatoes of 0.01 mg/kg, the calculated TMDI (Theoretical Maximum Dietary Intake), using the WHO European diet of adult consumers is 10% of the ADI. Calculations conducted for infants and toddlers in the United Kingdom and in Germany indicated chronic exposures ranging from 10 to 30% for these more vulnerable populations. These rough calculations concerns however potatoes only (the possible contribution of residues in bananas is not considered as this information is lacking) and it must also be kept in mind that the residue situation in potatoes needs to be clarified, in particular given that residue trials carried out in the North European region suggest that the situation in the South could be underestimated on the basis of the few available data.
As far as acute exposure is concerned, considering a residue level in potatoes of 0.01 mg/kg and a high unit to unit variability in the sample (variability factor of 7), the calculated NESTI (National

Short Term Intake Estimate) on the basis of British consumption data is about 30% of the ARfD for toddlers. Such acute intake assessment is not possible for bananas.
In conclusion it is currently not possible to draw a robust conclusion on the actual exposure of the consumer and on the actual risk for his health.

3.4. PROPOSED MRLS

At this stage there are insufficient residues trials available to propose MRLs for potatoes and bananas. The appropriate monitoring residue definition for bananas could not be concluded because of the identified deficiencies in the plant metabolism studies available at the time this conclusion was finalised (see section 3.1.1.). No MRLs are currently proposed for products of animal origin to due expected very low exposure of domestic animals. However this expectation would need to be validated should the results from the residues trials on potato identified as a data gap become available.

4. Environmental fate and behaviour

Cadusafos was discussed at an EPCO experts' meeting for environmental fate and behaviour (EPCO 26) in June 2005. The applied for intended use in southern Europe on potatoes was not critically peer reviewed by the experts from Member States at the EPCO meeting as the applicant had indicated they would not provide further data or information to support this use. The discussions at the peer review meeting therefore concentrated on the intended use on bananas. Comments and observations in this conclusion relating to the use on potatoes therefore originate from the EFSA or the RMS only. Consequently identified data gaps regarding the potato use are the views of the EFSA and the RMS only.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

In soil experiments carried out on 3 different soils under aerobic conditions in the laboratory (25 °C, 75% field capacity (FC) in the dark) dosed with butyl-2-^{14}C-cadusafos no major (>10% applied radioactivity (AR)) radiolabelled metabolites were formed. In one of the soils the metabolite methyl-2-butyl sulfone was present at 5.4%AR at 7 days and 7.5%AR at 14 days before declining to 2.75%AR by day 30. In the other 2 soils investigated it could not have been present at > 1.7%AR at any sampling time. The formation of residues not extracted by acetonitrile/water was a significant sink for the applied radiolabel (25-32% AR after 90-120 days). Mineralisation to CO_2 was the major sink for the applied radioactivity accounting for 43-70.9%AR after 90-120 days.

Under anaerobic conditions in soil, the route of degradation identified was essentially the same degradation pathway as described above for aerobic conditions with the rate of degradation being slower than under aerobic conditions in the soil tested. In a laboratory soil photolysis study, cadusafos was essentially stable.

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

In the aerobic soil degradation studies discussed in section 4.1.1. above cadusafos degraded with single first order DT_{50} of 12.3, 47.1 and 52.2 days (25 °C, 75% FC). In a further 4 different soils incubated in the laboratory in the dark at 20 °C and 40% maximum water holding capacity (MWC) these values were 50.9, 51.6, 62.1 and 62.3 days. When normalised to 20 °C and field capacity moisture content (-10kPa) according to FOCUS guidance[4], the range of laboratory values was 14.6-62 days with a geometric mean value of 38.3 days and median of 38.5 days. Under flooded anaerobic conditions in 1 soil at 2 5°C the single first order DT_{50} for cadusafos was 48.6 days. In the soil where the metabolite methyl-2-butyl sulfone was present above 5%AR at 2 consecutive time points a single first order DT50 of 4.5 days was estimated for methyl-2-butyl sulfone.

In field dissipation studies carried out at 3 trial sites in Southern Europe (2 sites in Spain and 1 in Italy) single first order DT_{50} for cadusafos (methyl-2-butyl sulfone was not analysed for) were 38, 59 and 12 days. In a single trial site in The Netherlands a 'best fit' DT_{50} of 46 days (DT_{90} 755 days) was calculated (details of the kinetic model utilised were provided in Addendum 2 to the DAR dated January 2006). The DT_{50} calculations appropriately took account of all soil layers where residues were detected (validated limit of quantification 0.007 mg/kg, 0-40 cm soil layers or at The Netherlands site 0-60 cm). Note the applied for intended uses were only for potatoes and bananas in southern Europe, so the results from the field trial in The Netherlands are not directly applicable to the applied for uses.

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

In guideline batch adsorption studies on 4 different soils K_foc values of 144-351 mL/g were determined for cadusafos (1/n 0.97-1.004) There was no evidence that adsorption was correlated with soil pH. The arithmetic mean values appropriate for use in FOCUS modelling were K_foc 227 mL/g and 1/n=0.988.

In a field leaching study in The Netherlands cadusafos was applied at 4.5 kg/ha to soil as a spray without incorporation just before a potato crop was planted in early May. Groundwater was sampled from sampling wells at ca. 1.7m (0.5m below the average level of the groundwater table of 1.2 m). During the experiment the groundwater table was as close to the soil surface as 0.7 m. Parent cadusafos was determined in these samples of groundwater at a maximum of 0.4 µg/L 270 days after application decreasing to 0.4µg/L 1 year after application. (Note, for information the 'best fit' soil dissipation DT_{50} determined for cadusafos at this trial site was 46days (DT_{90} 755 days)). The groundwater samples were not analysed for the soil metabolite methyl-2-butyl sulfone. Whilst these data indicate that under very vulnerable groundwater leaching conditions as found in the Netherlands

[4] Generic guidance for FOCUS groundwater scenarios version 1.1 dated April 2002. The individual values calculated by EFSA were 14.6, 32.3, 38.4, 38.5, 49.7, 55.9 & 62 days.

contamination of groundwater above the parametric drinking water limit of 0.1µg/L will occur, it should also be noted that use in northern Europe on potatoes was not an applied for intended use.

In a second field leaching study carried out near Sevilla in Spain, cadusafos was applied at 4 kg/ha to soil as a granule with incorporation over the top 10cm soil layer just before a tobacco crop was planted in mid May with a second spray application being made to the soil surface 45 days later at 2 kg/ha (total dose 6kg/ha was equivalent to N rate compared to the applied for intended use on potatoes in southern Europe). Aquifer water was sampled from sampling wells at ca. 3.5 m (0.5 m below the average level of the groundwater table of 3m) approximately tri monthly for up to 21 months after the first application. Parent cadusafos was determined in these samples with average concentrations (from the 12 wells within the treated plots) up to 0.025 µg/L (See Addendum 2 to the DAR dated January 2006). However in samples taken 45 days after the first application, (the day of the second application) the average concentration was 0.517 µg/L. In the control sample well located 30m outside the treated area a concentration of 0.205 µg/L was determined. The study authors proposed these positive findings in 45 day samples resulted from contamination via sampling equipment. This seems a plausible explanation as no natural precipitation occurred at the trial site over this 45 day period and the irrigation applied is unlikely to have taken the top soil moisture above field capacity. The groundwater samples were not analysed for the soil metabolite methyl-2-butyl sulfone. (Note, for information the single first order soil dissipation DT_{50} determined for cadusafos at this trial site was 38days.). In conclusion this study shows that at this trial site in southern Spain for the climatic conditions over the study duration, contamination by cadusafos of the shallow groundwater aquifer immediately below the test plot occurred, but concentrations were less than the parametric drinking water limit of 0.1 µg/L.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Cadusafos was stable to sterile aqueous hydrolysis at environmentally relevant pH and stable under sterile aqueous photolytic conditions. In 20 °C guideline dark laboratory aerobic sediment / water studies (2 systems investigated, 25cm water column overlaying 2.5cm depth sediment), cadusafos dissipated from the water with single first order DT_{50} of 36 and 38 days primarily by partitioning to sediment, volatilising and mineralising to CO_2. The breakdown product methyl-2-butyl sulfone was identified by co-chromatography with a certified reference standard but it never accounted for more than 0.9%AR in water or 0.17%AR in sediment extracts. In the whole system (excluding the cadusafos in the volatile traps) single first order DT_{50} were 59 and 68 days. At 100 days mineralisation to CO_2 accounted for 12-18%AR, volatilised cadusafos accounted for 24-28%AR, whilst residues not extracted from sediment by acetonitrile/water accounted for 6-8%AR.

For the applied for intended use on bananas in the Canary Islands, where application is made through drip irrigation systems the potential for contamination as a result of surface runoff was assessed using a scenario developed by the applicant that was based on the FOCUS R4 scenario cropped with citrus but had soil hydraulic properties parameterised for a soil specific to banana growing in Tenerife (See

Addendum 2 to the DAR dated January 2006). The FOCUS models were run using this re-parameterisation of the PRZM runoff model, linked to TOXSWA. The application rate assumed was 4 kg a.s./ha (lower than the applied for requested use of 6kg a.s./ha). This modelling calculated surface water concentrations of <0.001µg/L and sediment concentrations of <0.001 µg/kg dw. Whilst this modelling did not use a high enough application rate, as the infiltration capacity of the soil using this parameterisation of PRZM was predicted by PRZM not to be exceeded during the simulation, the same results would have been obtained had the higher application rate been simulated. As discussed below in section 4.2.2 the active substance properties: soil DT_{50} and Henry's law constant used as modelling input were also inappropriate. However, again, as the infiltration capacity of the soil was predicted not to be exceeded during the simulation, the same results would have been obtained had the appropriate active substance properties been used as input. The experts from Member States at the EPCO meeting were unable to conclude if the hydrological parameterisation of the model was appropriate based on the detail of information provided in the addendum. Clarification on the approach taken regarding the hydrological parameterisation of the scenario within the PRZM model was therefore requested. This detail is available in appendix I to the original study report[5] but is still not available in any addenda to the DAR. The EFSA considers that the hydrological parameterisation of this 'hybrid' scenario within PRZM was appropriate. It is therefore the EFSA's view that surface water exposure from the applied for intended use will be negligible when the product is used in Tenerife. This conclusion is specific to use in Tenerife and does not apply to banana growing elsewhere.

For the applied for intended use on potatoes in southern Europe initial PEC in surface water systems were (in the view of the EFSA) appropriately calculated for the spray drift route of entry to surface water as presented in the DAR. At later time points and for the time weighted average values the EFSA considers that a water dissipation DT_{50} of 38 days (and not 69 days as originally proposed in the DAR) is appropriate for use in calculations to a static water body (longest value from the lower of the 2 dosing regimes used in the studies, which still gave an exaggerated initial concentration of ca. 126µg/L). The drainage and runoff routes of entry to surface water systems have not been assessed. This is a data gap. However as there are potato growing situations in southern Europe where the runoff and drainage routes of entry will contribute little to surface water exposure it could be appropriate for this to be addressed by MS when carrying out national product authorisations.

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

For the applied for intended use on bananas the applicant developed a groundwater scenario using a soil description from the Canary Islands (Tenerife) that was more vulnerable to leaching than the standard FOCUS Sevilla scenario. This was implemented using 'User Specified Scenarios' in PELMO 3.2.2. With the exception of the parameterisation of the soil hydraulic properties this scenario used the definition of the FOCUS Sevilla scenario cropped with citrus (See Addendum 2 to

[5] Jarvis T 2005. Predicted environmental concentrations of cadusafos in surfacewater following use on bananas in the Canary Islands. Report number: FM22305-1

the DAR dated January 2006). The experts from Member States at the EPCO meeting were unable to conclude if the hydrological parameterisation of the model was appropriate based on the detail of information provided in the addendum. Clarification on the approach taken regarding the hydrological parameterisation of the scenario within the PELMO model was therefore requested. This detail is available in appendix I to the original study report[6] but is still not available in any addenda to the DAR. The EFSA considers that the hydrological parameterisation of this 'hybrid' scenario within PELMO was appropriate.

The EPCO peer review meeting also had reservations over the active substance properties selected as input to the modelling. The use of an adsorption K_{foc} of 227 mL/g and Freundlich slope (1/n) of 0.99 were considered appropriate. However the experts had reservations over the use of an arithmetic mean single first order field soil DT_{50} of 38 days from the available field dissipation studies. They were concerned that in the available field dissipation studies leaching to deeper soil layers and volatilisation may have contributed to the measured DT_{50} such that the values did not sufficiently represent degradation as is necessary when field DT_{50} are used as input to leaching modelling. As clarified at section 4.1.2, as the DT_{50} were estimated using measured residues in all soil layers where residues were detected, the contribution of leaching to deeper soil layers to the DT50 value would have been minimised. Therefore the field DT values were considered by EFSA to approximate to degradation rates (except that volatilisation cannot be excluded as contributing to dissipation, see section 4.3). The EFSA therefore consider that it could be appropriate to use field single first order soil DT_{50} values as input in the leaching modelling provided a Henry's law constant of 0 Pa. m^3 mol^{-1} was also used as input so volatilisation losses are not double counted. However in The Netherlands field trial (see section 4.1.2) the DT_{50} value of 46 days is not a first order value (DT_{90} 755 days). Therefore in accordance with agreed evaluation practice/FOCUS groundwater guidance either the longest (of 3 values) single first order field DT_{50} of 59 days (Spanish and Italian trials) should be used as modelling input (a proposal of the Member State experts at the EPCO meeting) or a geometric mean value of 50 days including the Netherlands trial but estimated in accordance with first order kinetics (755/3.32=227 days) (another option foreseen in FOCUS guidance) could be used. Of course as the field values in such an assessment have not be normalised to reference conditions the corrections for temperature and moisture content the PELMO model would need to be disabled.

Another alternative that would also comply with FOCUS guidance would be to use the geometric mean / median laboratory (20°C, -10kPa soil moisture) single first order DT_{50} of 38 days (see section 4.1.2) as input with corrections for temperature and moisture content enabled in the PELMO model.

Finally the groundwater modelling summarised in Addendum 2 to the DAR dated January 2006 assumed an application rate of 4 kg a.s./ ha (applied through drip irrigation systems at a rate of up to 4g per plant) which is not in accordance with the notified intended use of 6kg a.s./ha (applied through drip irrigation systems at a rate of up to 4g per plant).

[6] Jarvis T 2005. Predicted environmental concentrations of cadusafos in groundwater following use on bananas in the Canary Islands. Report number: FM22305-2

Therefore in order to exclude (or identify) the potential for groundwater contamination of cadusafos from the notified intended use on bananas in the Canary Islands further groundwater modelling is required.

For the applied for intended use on potatoes in southern Europe FOCUS groundwater modelling was reported in the original DAR. This modelling cannot be relied on as the single first order soil DT_{50} and Henry's law constant used as input were inappropriate[7]. Therefore to support this use on potatoes, further groundwater modelling would be required.

Based on the results of the field leaching study carried out in southern Spain as described in section 4.1.3, evidence is available that under the geoclimatic conditions represented by this field study, cadusafos when used in accordance with the applied for intended use on potatoes would not be expected to contaminate groundwater at a concentration above 0.1µg/L. This conclusion is specific to the soil type, climate and aquifer hydraulic conditions at the study site, a careful analysis would be necessary before the results measured at the study site could be extrapolated more generally to other southern European situations.

The metabolite methyl-2-butyl sulfone was present in a laboratory soil route of degradation study (see section 4.1.1) at two consecutive time points at >5%AR. Therefore in accordance with agreed guidance[8], its potential to contaminate groundwater must be further assessed. This data gap was identified by EFSA at the end of the peer review process. Whilst based on the available data methyl-2-butyl sulfone exhibits low persistence (see section 4.1.2) no information is available on its adsorption. This information would be required before a leaching assessment could be completed. The EFSA therefore considers that there is a data gap for the potential for the soil metabolite methyl-2-butyl sulfone to contaminate groundwater to be assessed.

4.3. FATE AND BEHAVIOUR IN AIR

Based on its vapour pressure (0.1196 Pa at 25 °C), cadusafos is classified as moderately volatile. Based on its Henry's Law constant (0.132 Pa. m^3. mol^{-1}, resulting in a dimensionless Henry's Law air water partition coefficient of $5.4x10^{-5}$ at 20 °C) it is classified as moderately volatile from aqueous systems. In laboratory natural sediment/water studies volatilisation was observed (0.76-0.85%AR in the first 48 hours increasing to 24-28%AR over 100 days). In a controlled atmosphere study (20 °C, 50% humidity, air velocity 1m.s^{-1}) where a CS formulation of cadusafos was incorporated into soil over the top 10 cm, measured volatilisation losses accounted for 1.3% of the applied dose over 48 hours. Cadusafos would not be expected to be subject to long range transport in the upper atmosphere, as using the method of Atkinson and the Atmospheric Oxidation Program (v.3.1) to

[7] The EFSA was also unable to reproduce the results reported in the draft assessment report even when using the same soil DT_{50} as the applicant (38 days). The EFSA simulations gave higher concentrations.
[8] 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 25 February 2003.

calculate photochemical reaction with hydroxyl radicals, a rate constant of $1.2x10^{-10}$ cm^3 $molecule^{-1}sec^{-1}$ was estimated. Assuming an atmospheric concentration of $1.5x10^6$ hydroxyl radicals cm^{-3} an atmospheric half life of 1.1 hours was calculated.

5. Ecotoxicology

Cadusafos was discussed at the EPCO experts' meeting for ecotoxicology (EPCO 27) in June 2005. The use in southern Europe on potatoes, originally applied for, was not critically peer reviewed by the experts from Member States as the applicant had indicated they would not provide further data or information to support this use. The discussion at the peer review meeting therefore concentrated on the intended use in banana plantations. Consequently comments and identified data gaps regarding the potato use are the views of the EFSA and the RMS only.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The risk to terrestrial vertebrates was assessed based on the use of 6 kg/ha cadusafos as soil directed broadcast application to potatoes or via irrigation system to banana plants. In the first tier assessment a small insectivorous bird was considered in accordance with the Guidance Document on Birds and Mammals (SANCO/4145/2000). TER values below the Annex VI trigger were obtained for the acute and long term, while the short term TER value was above. Since the use in potatoes was withdrawn by the applicant the refinements of the risk to birds from this use were not discussed in the experts' meeting. Neither was the risk to mammals from the use in potatoes discussed. For the use in banana it was agreed that the risk to birds and mammals should be based on species that occur in banana plantations and their associated diets. Furthermore, a justification of all refinement steps should be provided. Additional data was submitted by the applicant late in the evaluation process and was therefore not evaluated by the RMS or peer reviewed. Hence a conclusion on the risk to birds in banana plantations cannot be reached at this stage.

As cadusafos has a log Pow >3, and therefore a potential to bioaccumulate, the risk for secondary poisoning needs to be considered. The risk to earthworm-eating birds and mammals was calculated in the original DAR based on measured residues in earthworms from the reproduction laboratory study. A high risk was identified (TER=1.9 for birds; TER=0.06 for mammals) based on an application of 6 kg a.s./ha incorporated into a 5 cm soil layer which is relevant for the use in banana. For the use in potatoes incorporation into a 30 cm soil layer was used to calculate the PEC_s. This resulted in TER values of 7.6 and 0.24 for birds and mammals respectively. Considering the potential for bioaccumulation, residues in earthworms in the field might be higher due to lower organic content of natural soils compared to the artificial soil used in the laboratory study. It should also be noted that first tier TER values for earthworm-eating birds and mammals calculated according to SANCO/4145/2000 are much lower. Hence this should be considered when the risk is further addressed. The risk to fish-eating birds and mammals was assed in the original DAR and revised in Addendum 2 based on a PEC_{sw}, calculated from application of 6 kg a.s./ha and 2.77% spray drift to a 30 cm deep water body at 1 m distance. For fish-eating birds 15 m buffer zones would be required to

meet the Annex VI trigger for the use in potatoes. For mammals the TER value with a 30 m buffer zone was calculated to 0.87 (recalculated by the EFSA based on revised PEC_{sw} to 0.95), thus indicating a high risk. For the use in bananas the assessment was based on the conclusion of negligible contamination of surface water in the Tenerife-specific scenario (see section 4.2.1) and therefore the risk is considered to be low for this specific use. Since application to bananas is by drip irrigation to the soil, the risk due to exposure to contaminated drinking water is also considered low.

5.2. RISK TO AQUATIC ORGANISMS

Cadusafos is toxic to fish and aquatic invertebrates with an EC_{50} of 0.75 µg/L and a NOEC of 0.231 µ/L for *Daphnia magna*, the most sensitive of the species tested in single species tests. First tier acute and long-term TER values were calculated based on an application rate of 6 kg a.s./ha to potatoes and spray drift to a 30 cm deep water body at different distances from the field. The obtained values are below the Annex VI trigger with a buffer zone of 30 m, indicating a high risk. The risk to algae is considered low.

Cadusafos partitioned into sediment in the water/sediment studies. A risk to sediment-dwelling organisms was identified in the first tier assessment based on results from a sediment-spiked study with *Chironomus riparius.*

An available mesocosm study was discussed in the experts' meeting. It was agreed that the endpoint from this study should be 0.06 µg a.s./L. At this concentration some direct effects took 13 days to recover and indirect effects took 55 days to recover. Since no clear NOEC was obtained in the study, it was agreed that a safety factor of 3 should be applied for the proposed uses.

No major metabolites were detected in the water/sediment studies.

Since the proposed use in potatoes was withdrawn by the applicant, no refined assessment of the risk to aquatic organisms from this use was submitted. However, since the endpoint from the mesocosm study was lower than the NOEC for *Daphnia* in laboratory test, the risk to both fish and aquatic invertebrates is concluded to be high and needs to be further addressed.

For the use in banana plantations specifically in Tenerife the risk to aquatic organisms is considered low based on negligible contamination of surface water (see section 4.2.1).

The BCF for fish was determined to 220 and the level of radioactive residues in whole fish at 14 days of depuration was <95%, hence the risk for biomagnification in aquatic food chains is considered as low.

5.3. RISK TO BEES

Cadusafos is very toxic to bees. The HQ values calculated based on results from acute oral and contact laboratory studies are approximately 60 times the Annex VI trigger value of 50. However,

since cadusafos will only be applied to bare soil the risk to bees is considered low. A relatively limited amount of cadusafos is taken up in the plants, however there is the potential for other residues (not fully characterised) to be taken up (see section 3.1.2). Since banana is not flowering the risk to bees from plant residues is considered low.

5.4. RISK TO OTHER ARTHROPOD SPECIES

The results from laboratory studies with the standard species *Aphidius rhopalosiphi* and *Typhlodromus pyri* reflect the insecticidal activity of cadusafos, and clearly demonstrate that there is a risk to in-field non-target arthropods. Further semi-field tests were carried out, using both standard species and the soil dwelling species *Poecilus cupreus*. Tests with the two standard species were performed according to a dose-response design leading to a LR_{50}, and by using this value off-field HQs were calculated. The test with *Poecilus cupreus* was conducted with a single application rate of 4.5 kg a.s./ha, which is lower than the recommended maximum application rate of 6.0 kg a.s./ha. Mortality at 14 days was 82%, decreasing to 12.5% at days14-28. Results from additional semi-field tests with soil dwelling species (*Tachyporus hypnorum, Bembidiom lampros* and *Pardosa* spp.) using a granular formulation are available. Although a different formulation than the lead formulation was used, the results are indicative of a potential risk.

No in-field exposure of leaf dwelling species is expected from the evaluated uses. For the application of cadusafos by drip-irrigation to banana plants no off-field exposure is expected. The calculated HQ values for the broadcast soil application to potato fields show that 20 m buffer zones are required to protect non-target arthropods off-field. Since the test with *P. cupreus* was conducted at an application rate which is lower than the proposed, further testing with the appropriate rate and formulation is considered necessary in order to demonstrate a potential for in-field recolonisation and recovery. Since an off-field risk was identified for the potato use further studies with a second appropriate species is required. This could be addressed with the ongoing study with *Aleochara bilineata*. The experts' meeting also agreed that the study with *A. bilineata* should be submitted for the use in banana due to the perceived low sensitivity of *P. cupreus*.

5.5. RISK TO EARTHWORMS

No acute study with technical cadusafos is available. However the results from acute and reproduction studies with the formulation Rugby 200 CS show that cadusafos is toxic to earthworms. The TER values are 0.80 and 0.12 for acute and long term respectively in banana, which are clearly below the Annex VI triggers of 10 and 5, thus indicating a high risk. For the use in potato, the EFSA calculated the acute and long-term TER values to 4.8 and 0.69 respectively, based on incorporation into 30 cm soil. The experts' meeting agreed that the ongoing field study conducted in United Kingdom should be submitted and that the relevance for the proposed uses should be addressed. It should however be noted that the application rate in this study is 4.5 kg cadusafos per hectare, which is below the proposed application rate for the intended uses.

No major metabolites were detected in the soil degradation studies.

5.6. RISK TO OTHER SOIL NON-TARGET ORGANISMS

No studies on other soil non-target macro-organisms were submitted. However, further data are required since $DT_{90\ field}$ for cadusafos (in Southern Europe, where the proposed GAP is applicable) is >100 days, and a potential risk is expected due to direct exposure from bare soil application. This risk is also indicated by results from soil non-target arthropod studies. The experts' meeting agreed that a study with Collembola and mites is required to address the risk. No major metabolites were detected in the soil degradation studies.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

Cadusafos applied as a standard clay core type granule formulation at 10 kg a.s./ha, or 50 kg a.s./ha caused no statistically significant effects on soil microflora respiration and nitrogen transformations. All values were below the trigger value of ±25%, indicating that no effect is expected at the proposed use of cadusafos.

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

No data on effects on non-target flora and fauna are available. Cadusafos is expected to be toxic to fauna. For the drip irrigation use in banana no off-crop exposure is expected and therefore the experts' meeting agreed that no further data is needed. However, for the potato use the risk has to be addressed.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

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

6. Residue definitions

Soil

Definitions for risk assessment: cadusafos

Definitions for monitoring: cadusafos

Water

Ground water

Definitions for exposure assessment: cadusafos and methyl-2-butyl sulfone

Definitions for monitoring: cadusafos. Currently further fate and behaviour data are required before it can be concluded if methyl-butyl sulfone would also need to be included in a monitoring definition.

Surface water

Definitions for risk assessment: cadusafos

Definitions for monitoring: water cadusafos

sediment cadusafos

Air

Definitions for risk assessment: cadusafos

Definitions for monitoring: cadusafos

Food of plant origin

Definitions for risk assessment: potato, cadusafos; banana, available data insufficient to reach a conclusion.

Definitions for monitoring: potato, parent cadusafos; banana, available data insufficient to reach a conclusion.

Food of animal origin

Definitions for risk assessment: Due to expected low domestic animal intakes a definition is probably not required. However this expectation needs to be validated should the results from the residues trials on potato identified as a data gap become available.

Definitions for monitoring: The same as 'definition for risk assessment' above.

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Cadusafos	moderate to high persistence (single first order $DT_{50\ lab}$ = 15-62 d, 20°C -10kPa soil moisture); (single first order $DT_{50\ field}$ in s Europe = 12-59 d best fit $DT_{50}/DT_{90\ field}$ in n Europe = 46/755 d)	See sections 5.4 – 5.7

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
Cadusafos	K_{foc} 144-351 mL/g medium mobility	Acceptable modelling not available, data required	Yes	Yes	Yes
Methyl-2-butyl sulfone	Data gap for adsorption data exhibits low persistence	Assessment not available information required	No data available.	No data available.	No data available

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Cadusafos	See section 5.2

Air

Compound (name and/or code)	Toxicology
Cadusafos	Very toxic by inhalation (LC_{50} 0.026 mg/L)

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

- A new 5-batch analysis (data gap identified in the DAR and confirmed by the expert meeting, date of submission unknown, but applicant has announced during the evaluation meeting in February 2005 a study for May 2005, refer to chapter 1).
- Data on surface tension of Rugby 200 CS (data gap identified in the DAR and confirmed by the expert meeting, RMS has received a study but not evaluated, refer to chapter 1).
- Data regarding the shear rate at that the measurement of the viscosity has been conducted (datum gap identified at the evaluation meeting and confirmed by the expert meeting, date of submission unknown, but applicant has announced a study for May 2005, refer to chapter 1)
- Data on suspensibility and spontaneity of dispersion of Rugby 200 CS after freeze/thaw cycles (data gap identified in the DAR and confirmed by the expert meeting, RMS has received a study but not evaluated, refer to chapter 1).
- Data on the effectiveness of the cleaning procedure (data gap identified in the DAR and confirmed by the expert meeting, RMS has received a study but not evaluated, refer to chapter 1).
- Validation data for the method of analysis of cadusafos as manufactured (data gap identified in the DAR and confirmed by the expert meeting, RMS has received a study but not evaluated, refer to chapter 1).
- Precision and accuracy data for the method of analysis for the determination of the certain impurities in the technical material (data gap identified in the DAR and confirmed by the expert meeting, date of submission unknown, but applicant has announced a study for September 2005, refer to chapter 1).
- Accuracy data for the method of analysis for the determination of cadusafos in the representative formulation Rugby 200 CS (data gap identified in the DAR and confirmed by the expert meeting, date of submission unknown, but applicant has announced a study for May 2005, refer to chapter 1).
- ILV data for the methods of analysis for the determination of cadusafos residues in bananas (if the residue is cadusafos, only) and potatoes (data gap identified in the DAR and confirmed by the expert meeting, RMS has received a study but not evaluated, refer to chapter 1).
- Confirmatory method for the method of analysis for the determination of cadusafos residues in blood (data gap identified in the DAR and confirmed by the expert meeting, date of submission unknown, but applicant has announced a study for June 2005, refer to chapter 1).
- A validated analytical method for the determination of cadusafos residues in animal tissues (meat or liver) to address Annex point 4.2.5 of Directive 96/46/EC (date of submission unknown, data gap identified by EFSA after the expert meeting, refer to chapter 1).
- Potential short term inhalation toxicity of cadusafos has to be addressed (data gap identified by the expert meeting, date of submission unknown, refer to point 2.3).

- Applicant to submit a position paper on the toxicity of hydroxy-2-butane sulfonic acid (data gap identified by the expert meeting, position paper submitted to the RMS in January 2006 but not evaluated, refer to point 2.8).
- Applicant to provide batch analysis to confirm the level of the new impurity in the toxicological batches used for comparative toxicity testing (data gap identified by the RMS in an addendum, date of submission unknown, position paper submitted to the RMS in January 2006 but not evaluated, refer to point 2.8).
- Applicant to submit data relating to accidental and/or occupational exposure (data gap identified by the expert meeting, data of submission unknown, refer to point 2.9).
- Applicant to submit a new plant metabolism study to support the applied for representative use on banana, to include satisfactory metabolite identification and characterisation for a range of PHI's that are possible following the applied for use on bananas (label recommendations). These should include the shortest PHI, but also allow the evolution of the residue pattern with time to be elucidated; (data gap agreed at the meeting of experts, date of submission unknown; refer to point 3.1.1).
- Applicant to submit a full set of residues trials data that support the applied for representative use on banana. The residue to be analysed for in the trials will be dependant on the results from the banana metabolism study also identified as a data gap (data gap agreed at the meeting of experts, date of submission unknown; refer to point 3.1.1).
- Applicant to submit a further 4 residues trials data that support the applied for representative use on potato in southern Europe, analysing for cadusafos with an LOQ of 0.005mg/kg (data gap agreed at the meeting of experts. The applicant has indicated that use on potato is no longer supported; refer to point 3.1.1).
- Applicant to submit data to address the nature and levels of residues that have the potential to be taken up from soil by following crops, (to support the applied for representative use on potato in southern Europe; data gap identified in the DAR and confirmed at the meeting of experts. The applicant has indicated that use on potato is no longer supported; refer to point 3.1.2).
- The soil adsorption of methyl-2-butyl sulfone and its potential to contaminate groundwater must be appropriately assessed (relevant for all representative uses evaluated; data gap identified by the EFSA after the expert meeting, date of submission unknown, refer to point 4.2.2).
- FOCUS groundwater modelling for the potato use utilising appropriate cadusafos soil degradation and volatilisation input parameters (relevant for the Southern European potato use evaluated; data gap identified by the expert meeting. The applicant has indicated that use on potato is no longer supported; refer to point 4.2.2).
- PEC surface water and sediment from the potato use addressing the drainage and runoff routes of entry to surface water and a consequent aquatic risk assessment should be required by Member States when authorising products at the national level (relevant for the Southern

European potato use evaluated; data gap identified by the EFSA. The applicant has indicated that use on potato is no longer supported; refer to point 4.2.1).

- Groundwater modelling for the banana use utilising appropriate cadusafos soil degradation and volatilisation input parameters (relevant for the use evaluated on banana, specifically in Tenerife; data gap identified by the expert meeting, data available, not evaluated; refer to point 4.2.2).
- The risk to birds should be further addressed. For the use in banana, species that occur in banana plantations should be considered. The applicant has indicated that use on potato is no longer supported (data gap agreed in EPCO meeting; new information submitted late in the evaluation process and therefore not evaluated; refer to point 5.1)
- The risk to mammals should be further addressed. For the use in banana, species that occur in banana plantations should be considered. The applicant has indicated that use on potato is no longer supported (data gap agreed in EPCO meeting; new information submitted late in the evaluation process and therefore not evaluated; refer to point 5.1).
- The risk to fish should be further addressed (relevant for the use in potatoes; the applicant has indicated that use on potato is no longer supported; refer to point 5.2).
- The risk to aquatic invertebrates should be further addressed (relevant for the use in potatoes; the applicant has indicated that use on potato is no longer supported; refer to point 5.2).
- The risk to non-target arthropods should be further addressed with two relevant species in order to show the potential for in-field recolonisation and recovery (data gap agreed in EPCO meeting; relevant for the use in potatoes; the applicant has indicated that use on potato is no longer supported; refer to point 5.4).
- The risk to non-target arthropods should be further addressed with the ongoing study with *Aleochara* (data gap agreed in EPCO meeting; relevant for the use in banana; submission date unknown; refer to point 5.4).
- The risk to earthworms should be further addressed. The relevance of the ongoing field study conducted in UK should be addressed (relevant for both uses; study submitted late in the evaluation process and therefore not evaluated; refer to point 5.5).
- A study with a Collembola species and mites is required to address the risk to other soil macro-organisms (data gap agreed in EPCO meeting; relevant for both uses; submission date unknown; refer to point 5.6).
- A study on effects on non-target flora is required (relevant for the use in potatoes; the applicant has indicated that use on potato is no longer supported; refer to point 5.8).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative as insecticide and nematicide comprise the application by spraying or via the drip irrigation system to control a range of soil insects and nematodes in bananas and potatoes at application rates of up to 6 kg cadusafos per

hectare. In case of potatoes incorporation into soil takes place after the application. Cadusafos can be used as insecticide and nematicide. It should be noted that during the peer review process the applicant stated that only the use in bananas will be supported in the EU review process.
The representative formulated product for the evaluation was "Ruby 200 CS", a capsule suspension (CS). Preparations containing cadusafos are registered in Cyprus, France, Greece and Spain.

Adequate methods are available to monitor all compounds given in the respective residue definition only for soil, water and air, i.e. cadusafos in soil, water and air.
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.
Insufficient data are available for the determination of cadusafos in the technical material and in the representative formulation to ensure that quality control measurements of the plant protection product are possible.

The absorption of cadusafos is extensive and rapid, the excretion is mainly via urine, without evidence of body accumulation. The acute oral toxicity is high, and the acute inhalation and dermal toxicity are very high. The proposed classification is **T^+, R26/27 "Very toxic by inhalation and in contact with skin"; T, R25 "Toxic if swallowed".**
The main effect after short term oral administration is the decrease of cholinesterase activities in all species. Cadusafos has not genotoxic potential and is not considered to be carcinogenic. In the two-generation rat study, there was no effect on reproductive performance or fertility, and in the rat and rabbit teratology studies, no evidence of teratogenic effects in the absence of maternal toxicity.
Supplementary studies were performed due to the introduction of a new impurity in the technical material. The acute and subchronic oral tests revealed no difference in toxicity. The Ames test was negative.
The Acceptable Daily Intake (ADI) is 0.0004 mg/kg bw/day, the Acceptable Operator Exposure Level (AOEL) is 0.0007 mg/kg bw/day, and the Acute Reference Dose (ARfD) is 0.003 mg/kg bw/day. The comparison of the oral and dermal LD_{50} values results in a dermal absorption value of 100%. **The operator exposure estimates are based solely on one specific and restricted representative use in bananas**, with automatic drip irrigation, work rate of 1 ha/day, application rate of 6 kg a.s./ha, and assuming that the microcapsules in the formulation do not release cadusafos until they are diluted for application. The results are below the AOEL according to the currently used models which do not apply properly to this particular scenario. Worker and bystander exposures are expected to be very low due to the mode of application by drip irrigation.

The metabolism of cadusafos has been investigated on several crops after soil application.
The representative use on potatoes can be considered as adequately covered by these data and the residue definition for this use can be cadusafos only, for both monitoring and risk assessment. The available residue trials in potatoes for Southern Europe are however not sufficient to draw a robust conclusion on the residue levels consumers may be exposed to. The available data suggest that

residues are below 0.01 mg/kg, but results from trials in Northern Europe indicate that the currently available data may underestimate the actual situation. Further supervised residue trials should be carried out.
For the representative use on bananas, although 2 metabolism studies for this crop were submitted, the data are not sufficient to propose a residue definition. This is due to major deficiencies in the studies, making it impossible to evaluate the possible presence of degradation products still exhibiting the anticholinesterase activity of the parent compound. Therefore a new metabolism study in bananas is needed as well as residue trials carried out according to the representative use pattern. The compounds to be analysed in the residue trials should be determined on the basis of the results of the metabolism study.
The situation for rotational crops has not been addressed by the notifier, although the soil persistence of the compound exceeds the trigger value for conducting uptake and metabolism studies in succeeding crops. Therefore these studies should be requested.
Based on the current knowledge of the residue situation in potatoes, the exposure of livestock is very low and metabolism studies in domestic animals do not need to be carried out.
Only preliminary acute and chronic exposure assessments could be conducted for the use on potatoes, but these assessments need to be re-examined on the basis of complete and robust data. No MRLs can be proposed at this stage.

The information available on the fate and behaviour in the environment is generally sufficient to carry out an appropriate environmental exposure assessment at the EU level with the following notable exceptions. For the use on potato the drainage and runoff routes of exposure to surface water have not been covered for cadusafos in the available EU level assessment. This exposure assessment and the associated risk assessment to aquatic organisms should be completed in national assessments made by the Member States. Whilst an acceptable surface water exposure assessment for the banana use in Tenerife that identified negligible exposure is available, this is a very specific assessment applicable to just this location, so it should not be used to support authorisations on bananas in other locations. For the notified intended uses on both potato in s Europe and banana the potential for groundwater exposure by cadusafos or its soil metabolite methyl-2-butyl sulfone cannot be concluded. Further information is required to complete the groundwater assessment.

In the first tier assessment an acute and long-term risk was identified for insectivorous birds. A risk was also identified for earthworm-eating birds and mammals as well as for fish-eating birds and mammals for the use in potatoes. Since the use in potatoes was withdrawn by the applicant the refinements of the risk to birds and mammals from this use was not further considered. For the use in banana plantations a conclusion on the risk to birds and mammals can not be reached at this stage. The risk needs to be further addressed based on species that occur in banana plantations and their associated diets.

Cadusafos is very toxic to fish and aquatic invertebrates. The assessment indicates a high risk. However, for the specific use in banana plantations in Tenerife the risk to aquatic organisms is considered low based on negligible contamination of surface water.

The toxicity to bees is high, but since for the proposed uses application will be to bare soil the risk is considered low. No in-field exposure of leaf dwelling non-target arthropods is expected from the evaluated uses. The available test with *Poecilius cupreus* was conducted at an application rate which is lower than the proposed. An ongoing study with *Aleochara bilineata* should be submitted for the use in banana due to the perceived low sensitivity of *P. cupreus*. For the application of cadusafos by drip-irrigation to banana plants no off-field exposure is expected.

A high acute and long-term risk was identified for earthworms. The ongoing field study conducted in United Kingdom should be submitted and the relevance for the proposed uses should be addressed. It should however be noted that the application rate in this study is 4.5 kg cadusafos per hectare, which is below the proposed application rate for the intended uses. A study with Collembola and mites is required to address the risk to other soil macro-organisms. The risk to soil micro-organisms and biological methods of sewage treatment plants is low. For the drip irrigation use in banana no off-crop exposure is expected and the hence risk to non-target plants is considered low.

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

- Use of gloves by operators during mixing and loading.

Critical areas of concern

- For the moment no final specification for the technical material can be set (refer to chapter 1)
- Not sufficient data are available to ensure that quality control measurements of the plant protection product are possible (refer to chapter 1)
- Very high acute toxicity by inhalation, high acute oral and dermal toxicity.
- The potential of short term toxicity by inhalation needs to be addressed due to the very high acute toxicity by inhalation.
- The estimated operator exposure is below the AOEL for a restricted representative use:
  - automatic drip irrigation in bananas plantation
  - use of gloves during mixing/loading
  - work rate of 1 ha/day
  - assuming that the microcapsules in the formulation are stable until they are diluted during mixing and loading (this means no release of "free" cadusafos above 1.12%)
- The application of the standard models to this particular scenario implies inherent uncertainties.
- A consumer risk assessment cannot be completed because the available data does not enable the nature and potential level of residues in banana and the potential level of residues in potato and in crops grown following potato to be adequately concluded.

- A conclusion on the potential for groundwater exposure for parent cadusafos and the soil metabolite methyl-2-butyl sulfone cannot be made with the currently available information.
- For the intended use in potatoes the environmental exposure assessment and consequent risk to non-target organisms was not critically peer reviewed by the Member States as the applicant indicated that further data or information to support this use will not be provided. A conclusion on critical areas of concern for this use could therefore not be reached.
- A first tier risk to birds was identified. Additional information is needed for birds that occur in banana plantations and the risk assessment should be based on these species and their specific diets.
- A first tier risk to earthworm-eating mammals was identified. Additional information is needed for mammals that occur in banana plantations and the risk assessment should be based on these species and their specific diets.
- The first tier assessment indicates a high risk to non-target arthropods. No conclusion on the potential for recolonisation and recovery can be drawn without evaluation of additional data.
- A high acute and long-term risk to earthworms was indicated in the first tier assessment. An ongoing field study and its relevance for the intended use needs to be evaluated.
- No studies are available to assess the risk to other soil non-target arthropods.

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

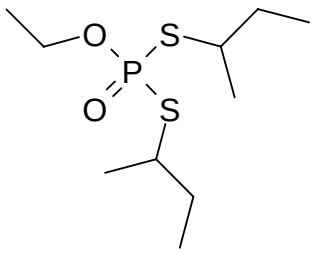
(Abbreviations used in this list are explained in appendix 2)

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

Active substance (ISO Common Name) ‡	Cadusafos
Function (e.g. fungicide)	Insecticide and nematicide

Rapporteur Member State	Greece
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	*S*,*S*,-di-*sec*-butyl *O*-ethyl phosphorodithioate
Chemical name (CA) ‡	O-ethyl S,S-bis (1-methylpropyl) phosphorodithioate
CIPAC No ‡	682
CAS No ‡	95465-99-9
EEC No (EINECS or ELINCS) ‡	Not available
FAO Specification ‡ (including year of publication)	Not available
Minimum purity of the active substance as manufactured ‡ (g/kg)	900 g/kg *(a new 5-batch-analysis study is on going)*
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	None
Molecular formula ‡	$C_{10}H_{23}O_2PS_2$
Molecular mass ‡	270.4
Structural formula ‡	

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

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	No solidification was observed; Freezing point < - 65 °C (pure 98.1%)
Boiling point (state purity) ‡	114-115 °C at 107 Pa (pure 98.1%)
Temperature of decomposition	Not relevant
Appearance (state purity) ‡	pure a.s. (98.1%): clear colourless liquid at room temperature technical a.s. (91.9%): yellow liquid at room temperature
Relative density (state purity) ‡	Density: 1.052 g/mL at 25 °C (pure 98.1%)
Surface tension	42.2 mN/m at 20 °C and concentration 197 mg/L (technical 90.9%) 43.3 mN/m at 25 °C and concentration 184 mg/L (pure 98.1%)
Vapour pressure (in Pa, state temperature) ‡	1.196×10^{-1} Pa at 25 °C (technical 94.2%)
Henry's law constant (Pa m^3 mol^{-1}) ‡	1.32×10^{-1} Pa m^3 mol^{-1} at 25 °C
Solubility in water ‡ (g/L or mg/L, state temperature)	245 mg/L at 25 ºC (pure 98.1%) pH was not reported; it was stated that pH was neutral.
Solubility in organic solvents ‡ (in g/L or mg/L, state temperature)	At 25 °C heptane: 125 g/kg methanol >250 g/kg o-xylene, 1,2-dichloroethane, acetone, ethyl acetate: miscible (solubilities expressed as g/kg solvent)
Partition co-efficient (log POW) ‡ (state pH and temperature)	log K_{ow} = 3.85 at 20.5 °C, in distilled water (pH 5.5) (technical 90.9%)
Hydrolytic stability (DT50) ‡ (state pH and temperature)	At 25 °C pH 5: stable pH 7: stable pH 9: DT_{50}=178.9 days
Dissociation constant ‡	Not relevant given the chemical structure.
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	In neutral medium (CH_3OH): λmax (nm) ε (Lxmole-1×cm-1) 224 884 No significant absorbance at or above 290 nm.
Photostability (DT_{50}) ‡ (aqueous, sunlight, state pH)	DT_{50}= 174 days at pH 8.1 (natural sunlight)

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

Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	Not relevant due to the low photochemical degradation
Flammability ‡	Non-flammable (technical 90.9%) Self-ignition temperature: 270 °C (technical 90.9%)
Explosive properties ‡	Non- explosive (technical 90.9%)

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

List of representative uses evaluated*

Crop and/or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
(a)			(b)	(c)	Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg a.s./hl min max	Water l/ha min max	kg a.s./ha min max	(l)	(m)
Potato	Spain	Rugby 200 CS	F	*Meloidogyne spp.; Globodera pallida, Globodera rostochiensis; Agriotes spp.; Agrostis spp.*	CS	200 g/L	broadcast, ground-directed spraying followed by incorporation over 30cm	Pre-planting	1	NA	2-3	200	4-6kg a.s./ha		(1)
Bananas	Spain	Rugby 200 CS	F	*Meloidogyne spp.; Radophilus similis; Tratylenchus spp.; Agriotes spp.; Agrostis spp*	CS	200 g/L	Through drip irrigation system	Spring or Autumn	1	NA	0.0125	48000	2- 4 g a.s./ mat (plant) ie 6 kg a.s./h a	15	(2)

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

Crop and/or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks
(a)			(b)	(c)	Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg a.s./hl min max	Water l/ha min max	kg a.s./ha min max	(l)	(m)
Potato	Greece	Rugby 200 CS	F	*Criconemoides spp, Helicotylencus spp., Phthorimaea operculella, Noctuidae, Meloidogyne spp., Elateridae, Tylenchorhychus spp.*	CS	200 g/L	broadcast, ground-directed spraying followed by incorporation over 30cm	Pre-planting	1	NA	2.5	200	5 kg		(1)

BI = Broadcast spray to bare soil followed by incorporation into soil
BS = Broadcast spray to bare soil without incorporation
Pre = Pre-sowing
Post = Post sowing
A = Autumn , S= Spring, NA = Not applicable

(1) The risk assessment for the use on potatoes was not finalised as it was withdrawn during the peer-review process by the notifier with respect to the evaluation for inclusion in Annex I.
(2) The risk assessment revealed first tier risks and data gaps in section 5 and data gaps in section 4.

Remarks:	*	Uses for which risk assessment could not been concluded due to lack of essential data are marked grey	(h)	Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated

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

	(a)	For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)	(i)	g/kg or g/L
			(j)	Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
	(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)	(k)	The minimum and maximum number of application possible under practical conditions of use must be provided
	(e)	GCPF Codes - GIFAP Technical Monograph No 2, 1989		
	(f)	Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench	(l)	PHI - minimum pre-harvest interval
	(g)	All abbreviations used must be explained	(m)	Remarks may include: Extent of use/economic importance/restrictions

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

Appendix 1.2: Methods of Analysis

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

Technical as (principle of method)	GC/FID Method inadequately validated (Linearity, precision and accuracy data required).
Impurities in technical as (principle of method)	GC/FID Method inadequately validated for the certain impurities (Precision and accuracy data required)
Plant protection product (principle of method)	GC/FID Accuracy data not provided

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Std No RAN-0314M: Substrates: banana (pulp, pulp+peel), potato tubers, green beans, melons, peppers, strawberries Extraction: Blending the processed sample with a methanol/water mixture, filtering and partitioning with methylene chloride Clean up: Filtration, concentration, addition of hexane. Further clean-up using silica gel SEP PAK Analysis: GC/FPD. Confirmation by GC/MSD Determined analyte: cadusafos LOQ: 0.005 mg/kg for all substrates except for banana pulp, for which LOQ is 0.001 mg/kg Method can be used for enforcement purposes, if ILV data are provided and cadusafos is the target compound. Std No. A-17-99-33: Substrates: potato tubers Extraction: Blending the processed sample with a methanol/water mixture, filtering and partitioning with methylene chloride Clean up: Filtration, concentration, addition of hexane. Further clean-up using silica gel SEP PAK Analysis: GC/NPD. Confirmation by GC/MSD Determined analyte: cadusafos LOQ: 0.002 mg/kg

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

	Method can be used for enforcement purposes, if ILV data are provided. Std No A-17-00-46: Substrates: banana pulp, tomatoes Extraction: Blending the processed sample with a methanol/water mixture, filtering and partitioning with methylene chloride Clean up: Filtration, concentration, addition of hexane. Further clean-up using silica gel SEP PAK Analysis: GC/NPD. Confirmation by GC/MSD Determined analyte: cadusafos LOQ: 0.005 mg/kg Method can be used for enforcement purposes, if ILV data are provided and cadusafos is the target compound.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not submitted but not required (No MRLs has been set for products of animal origin)
Soil (principle of method and LOQ)	Std No. 010.51091-2899: Substrates: soil, sediment, surface and groundwater Extraction: Acetone extraction Clean up: SPE or direct extraction for soil samples, LLE for sediment samples, SPE or LLE for water samples Analysis: GC/MS Determined analyte: cadusafos LOQ: 0.007 mg/kg for soil, 0.009 µg/L for surface water, 0.18 µg/L for groundwater
Water (principle of method and LOQ)	Std No. 010.51091-2899: Substrates: soil, sediment, surface and groundwater Extraction: Acetone extraction Clean up: SPE or direct extraction for soil samples, LLE for sediment samples, SPE or LLE for water samples Analysis: GC/MS Determined analyte: cadusafos LOQ: 0.007 mg/kg for soil, 0.009 µg/L for surface water, 0.18 µg/L for groundwater Std No. A-17-94-10: Substrates: distilled water, groundwater

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

	Extraction: Blending the processed sample with a methanol/water mixture, filtering and partitioning with methylene chloride Clean up: Filtration, concentration, addition of hexane. Further clean-up using silica gel SEP PAK Analysis: GC/NPD. Confirmation by GC/MSD Determined analyte: cadusafos LOQ: 0.1 µg/L for groundwater Std No. 010.51091: Substrates: surface water, tap water Extraction: The water samples are extracted using SPE cartridges Analysis: GC/MS Determined analyte: cadusafos LOQ: 0.05 µg/L for surface water
Air (principle of method and LOQ)	Std No. A-17-00-45: Substrates: air Extraction: Air was passed through adsorption filters which were extracted with hexane using a Soxhlet extraction Analysis: GC/NPD Determined analyte: cadusafos LOQ: 9 ng/m^3
Body fluids and tissues (principle of method and LOQ)	Std No. A-17-00-47: Substrates: human urine, human blood Extraction: Extraction with a methanol/water mixture. Partitioning with dichloromethane. Clean-up: SPE Analysis: GC/NPD Determined analyte: cadusafos LOQ: 0.005 mg/L *A confirmatory method and a method for animal tissues (liver or meat) are required.*

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	Not classified

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

Appendix 1.3: Impact on Human and Animal Health

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

Rate and extent of absorption ‡	Rapid and nearly complete > 80%, 168 hours following single oral low administration at 1 mg/kg bw
Distribution ‡	Widely distributed; highest concentration in liver, fat, kidneys and lungs
Potential for accumulation ‡	No evidence
Rate and extent of excretion ‡	Rapid and higher than 90% at 168 hrs, mainly *via* urine (63-78%), secondary *via* the expired air ($^{14}CO_2$) (11-17%), regardless of sex or route or mode of administration
Metabolism in animals ‡	Extensively metabolized, *via* cleavage of the thio-(sec-butyl) or O-ethyl- groups, oxidation and methylation. The majority of the identified metabolites were detected in urine.
Toxicologically relevant compound ‡ (animals and plants)	Parent compound (cadusafos) The toxicity of the plant metabolite hydroxyl-2-butane sulfonic acid, identified in banana peel, not known (no toxicology data available)
Toxicologically relevant compounds ‡ (environment)	Parent compound (cadusafos)

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	30.1 mg/kg bw, females	**R25**
Rat LD_{50} dermal ‡	10.7 mg/kg bw, females	**R27**
Rat LC_{50} inhalation ‡	0.026 mg/L air, females	**R26**
Skin irritation ‡	Non irritant	
Eye irritation ‡	Non irritant	
Skin sensitization ‡ (test method used and result)	Non sensitizer (Buehler)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Decreased RBC cholinesterase activity
Lowest relevant oral NOAEL / NOEL ‡	0.067 mg/kg bw/day (90-day, rat)
Lowest relevant dermal NOAEL / NOEL ‡	No data - not required
Lowest relevant inhalation NOAEL / NOEL ‡	No data available, justification required

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

Genotoxicity ‡ (Annex IIA, point 5.4)

……	Cadusafos is unlikely to be genotoxic

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

Target/critical effect ‡	RBC cholinesterase inhibition, decreased locomotion (females)
Lowest relevant NOAEL / NOEL ‡	0.045 mg/kg bw/day (rat chronic toxicity study)
Carcinogenicity ‡	Cadusafos is unlikely to pose a risk to humans

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	No reproductive toxicity effects. Decreased body weight gain (F1) and RBC cholinesterase activity (F0 & F1) at 0.262 mg/kg bw/day (rat)
Lowest relevant reproductive NOAEL/NOEL ‡	0.026 mg/kg bw/day (rat) (parental) > 0.371 mg/kg bw/day (rat) (reproductive) > 0.371 mg/kg bw/day (rat) (offspring)
Developmental target / critical effect ‡	No teratogenic or fetotoxic effects at non maternally toxic doses (rat, rabbit)
Lowest relevant developmental NOAEL / NOEL ‡	Parental: Rat: 6 mg/kg bw/day Rabbit: 0.3 mg/kg bw/day Developmental: Rat: 6 mg/kg bw/day Rabbit: > 0.9 mg/kg bw/day

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

Acute neurotoxicity ‡	NOAEL = 0.02 mg/kg bw (LOAEL = 25 mg/kg bw)
Repeated neurotoxicity ‡	NOAEL = 0.03 mg/kg bw/day
Delayed neurotoxicity ‡	No evidence of delayed neuropathy, NOAEL = 8.0 mg/kg bw/day

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

Other toxicological studies ‡ (Annex IIA, point 5.8)

Mechanism studies	No data - not required
Studies performed on metabolites or impurities	1) acute oral toxicity of cadusafos containing the impurity *o,o-diethyl S-sec-butyl phosphorothioate* LD_{50} = 38.9 mg/kg bw, female rats LD_{50} = 131.1 mg/kg bw, male rats

Medical data ‡ (Annex IIA, point 5.9)

…….	Limited, justification required

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.0004 mg/kg bw/day	2-year rat study	100
AOEL ‡	0.0007 mg/kg bw/day	90-day feeding study in rats	100
ARfD ‡ (acute reference dose)	0.003 mg/kg bw/day	Rabbit developmental study	100

Dermal absorption (Annex IIIA, point 7.3)

Rugby 200 CS	Concentrate: 100% Spray dilutions: 100% Based on the criteria set out in the Guidance Document on Dermal Absorption (Sanco/222/2000 rev.6)

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

Acceptable exposure scenarios (including method of calculation)

Operator	The exposure levels are lower than the AOEL for the proposed restricted use of Rugby 200CS on bananas, with an application rate of 6 kg a.s./ha and the following requirements : use of gloves automatic drip irrigation treated area : 1 ha/day assuming that the microcapsules are stable before dilution

	No PPE	PPE	
German:	352	11%	of AOEL
UK POEM, 5L	334	17%	of AOEL
UK POEM, 20L	559	28%	of AOEL

Workers	Worker exposure levels lower than the AOEL.
Bystanders	Bystander exposure levels lower than the AOEL.

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	T^+;	Very toxic
	R26/27	Very toxic by inhalation and by contact with skin
	R25	Toxic if swallowed

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

Appendix 1.4: Residues

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

Plant groups covered	Potatoes and radish (root vegetables (R)) Supporting information: corn (cereals(C)) A metabolism study in bananas in accordance with the representative use is required
Rotational crops	None
Plant residue definition for monitoring	Cadusafos (only for potatoes)
Plant residue definition for risk assessment	Cadusafos (only for potatoes)
Conversion factor (monitoring to risk assessment)	None

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

Animals covered	Probably not applicable since the intended uses of cadusafos do not lead to significant (>0.1 mg/kg of total diet) residues in livestock feed, but this would need to be confirmed once the residues trials database on potato is completed
Animal residue definition for monitoring	Not applicable
Animal residue definition for risk assessment	Not applicable
Conversion factor (monitoring to risk assessment)	Not applicable
Metabolism in rat and ruminant similar (yes/no)	Not applicable
Fat soluble residue: (yes/no)	Not applicable

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

……	DT_{50} ranging from 12.3 up to 62.3 days (Mean $DT_{50\ (20°C)}$ = 56.3 days) DT_{90} values ranged from 41.0 to 206.8 days Therefore, studies allowing identification and (eventually) quantification of residue in rotational crops are required.

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

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

……	Cadusafos residues can be retained in frozen conditions (- 18°C) for at least 15 months and the compound will remain stable in various plant matrices, including potatoes and bananas

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

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: no	Poultry: no	Pig: no
Muscle	Not applicable	Not applicable	Not applicable
Liver	Not applicable	Not applicable	Not applicable
Kidney	Not applicable	Not applicable	Not applicable
Fat	Not applicable	Not applicable	Not applicable
Milk	Not applicable		
Eggs		Not applicable	

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

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

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL	STMR (b)
Potatoes	Mediterranean	4X<0.01*	Further data required before MRL can be proposed	Data not sufficient to conclude	Data not sufficient to conclude
Bananas	Mediterranean	No data available	A complete set of data is required before MRL can be proposed	Data not sufficient to conclude	Data not sufficient to conclude

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

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

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

ADI	0.0004 mg/kg b.w./day
TMDI (European Diet) (% ADI)	Contribution of potatoes: 10% of ADI
TMDI (National Diet) (% ADI)	Contribution of potatoes: 13 – 28% of the ADI for infants, toddlers and children in the United Kingdom and in Germany
Factors included in NEDI	Not relevant
ARfD	0.003 mg/kg b.w./day
Acute exposure (% ARfD)	Potatoes: 50 and 35 % of ARfD for infants and toddlers respectively based on UK consumption data

Note: the calculations provided here above are to be considered as preliminary because they are based on an insufficient number of supervised residue trials.

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Not applicable since no analytical determinable residues occur in any of the raw commodities			

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

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

Potatoes	Data insufficient to propose MRLs
Bananas	Data insufficient to propose MRLs

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

Appendix 1.5: Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	Max. 43-70.9 % AR (after 90-120 days)
Non-extractable residues after 100 days ‡	Max. 25-32 % AR (after 90-120 days)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	None (Methyl sec-butyl sulfone: Max. 7.46 % AR at 14th day) above 5%AR at 7-14 days

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

Anaerobic degradation ‡	Mineralisation: (Max.: 44.7 % AR at 37-day post flood). Non-extractable residues: (Max.: 28.2 % AR at 37-day post flood). Metabolites: No major metabolites (Methyl 2-butyl sulfone: Max. 6.3 % AR (0-day post flood))
Soil photolysis ‡	No degradation after 30 days (Parent: 98.3 % AR after 30 days)

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

Method of calculation	Laboratory: single 1st order kinetics (Solver Function/ Microsoft® Excel 2000) Field studies: 1st order kinetics (Model Manager software package) except NL site where 'best fit' was used
Laboratory studies ‡ (range or median, with n value, with r^2 value)	Parent DT_{50lab} (20°C, aerobic): 50.9- 62.3 d (n= 4, r^2 = >0.87), DT_{50lab} (25°C, aerobic): 12.3- 52.2 d (n= 3, r^2 = >0.87) For FOCUS modeling, cadusafos: geometric mean and median DT_{50lab} 38 d (normalisation to pF2, 20°C, aerobic, first order kinetics); No specific effect noticed upon soil types.

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

	Parent DT_{90lab} (20°C, aerobic): 169.1- 206.8 d (n= 4, r^2 = >0.87) DT_{90lab} (25°C, aerobic): 41.0- 173.3 d (n= 3, r^2 = >0.87)
	$DT_{50lab(extrapol)}$ (10°C, aerobic): 40.5- 171.4 d (n= 8), ($DT_{50\ (10°C)} = DT_{50(20°C)} * Q_{10} = DT_{50(20°C)} * 2.2$)
	$DT_{50lab(extrapol)}$ (20°C, anaerobic): 72.5 d (n= 1), (Extrapolation from existing data at 25 °C: $DT_{50(T1)} = DT_{50(T2)} * e^{0.08*(T2-T1)}$ (where T1= 20°C and T2= 25°C)
	Degradation in the saturated zone: no data submitted and no data required.
Field studies ‡ (state location, range or median with n value)	DT_{50f}: Italy, 12 d (n= 1, r^2=0.978) Spain, 38-59 d (n= 2, r^2=0.838-0.988) Netherlands, 48 d (n= 1, r^2=0.905). Estimated 1st order value NL trial 227 days (DT_{90}/3.32) For FOCUS modelling – Parent: geometric mean 1st order DT_{50f} 50 d note this value has not been normalised to reference conditions.
	DT_{90f}: Italy, 41 d (n= 1, r^2=0.978) Spain, 127-197 d (n= 2, r^2=0.838-0.988) Netherlands, 755 d (n= 1, r^2=0.905)
Soil accumulation and plateau concentration ‡	DT_{90f} in Southern Europe less than 1 year both in lab. and field

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡	K_{oc}: Parent 144 – 351mL/g (mean 227mL/g), $^1/_n$= 0.97 – 1.004, 4 soils
K_d ‡	K_d : Parent 2 -6mL/g (mean 3.75mL/g, 4 soils)
pH dependence ‡ (yes / no) (if yes type of dependence)	No pH dependence *For FOCUS modelling – K_{foc}: Parent, mean 227mL/g, $^1/_n$= 0.988.

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

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

Column leaching ‡	data not available, not required
Aged residues leaching ‡	1st study Aged for (d): 30 d Precipitation (mm): 200 mm Time period (d) : 48 hour-period Leachate: less than 0.03 % of applied radioactivity in leachate 2nd study Aged for (d): 102 d Precipitation (mm): 200 mm Time period (d): 48 hour-period Leachate: no parent found in the leachate. 8 degradates of cadusafos were detected in the leachate. Of these compounds only one exceed 2% of applied radioactivity although in total, radioactivity in leachates accounted for about 8 %. The major degradate accounted for 5.5 % of applied radioactivity. The compound was identified as 2-butanesulfonic acid.
Lysimeter/ field leaching studies ‡	In southern Europe (Sevilla Spain) field leaching study on tobacco at 6kg/ha no leaching > 0.025µg/L was measured up to 540 d after application in a groundwater aquifer which was on average 3m below the soil surface of the treated plots.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	DT_{50} (d): 59 days (max value for South. Europe) Kinetics: 1st order Field or Lab: Field Soil density: 1.5 g/cm^3 Incorporation depth: 0.05 (banana) or 0.30 (potato) [1/] [1/] *Incorporation depth of 0.3 m instead of 0.2 m, as recommended by the Guidance Document 7617/VI/96 (29/2/97), was assumed because cadusafos is intended to be incorporated at 0.3 m soil depth (see relevant point B.3.3 Summary of data on application, page 24-Annex B).*

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

Application rate	Crop: Potato and Banana % Plant interception: (1) Potato: Pre-emergence therefore no crop interception, (2) Banana: Pre-emergence, drip irrigation Number of applications: 1 Interval (d): Not relevant Application rate(s): 6000 g a.s./ha potato and banana

Crop: Potato, Application dose: 6000 g a.s./ha, Inc. depth: 0.3 m

$PEC_{(s)}$ (mg/kg)	Single application Actual (DT_{50}: 59 d)	Single application Time weighted average (DT_{50}: 59 d)	Multiple application Actual	Multiple application Time weighted average
Initial	1.3	1.3	Not applicable	Not applicable
Short term 24h	1.28	1.29		
2d	1.27	1.28		
4d	1.24	1.27		
Long term 7d	1.19	1.24		
21d	1.01	1.15		
28d	0.93	1.10		
50d	0.72	0.98		
100d	0.40	0.76		

Crop: Banana, Application dose: 6000 g a.s./ha, Inc. depth: 0.05 m

$PEC_{(s)}$ (mg/kg)	Single application Actual (DT_{50}: 59d)	Single application Time weighted average (DT_{50}: 59 d)	Multiple application Actual	Multiple application Time weighted average
Initial	7.8	7.8	Not applicable	Not applicable
Short term 24h	7.69	7.73		
2d	7.60	7.69		
4d	7.42	7.60		
Long term 7d	7.16	7.47		
21d	6.08	6.89		
28d	6..0	6.63		
50d	4.32	5.88		
100d	2.40	4.58		

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

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) ‡	pH5: stable
(state pH and temperature)	pH7: stable
	pH9: 25°C , stable a slight degradation was observed (about 10% of the applied radioactivity). No degradation products formed at more than 10% of the applied radioactivity, except one about 10 % at pH 9 : the O-ethyl-S-(2-butyl) phosphorothioic acid (OSPA).
Photolytic degradation of active substance and relevant metabolites ‡	Stable, DT_{50}: 174 days The photodegradation products are all more polar than the parent compound and are mainly the phosphorothioic acid and the phosphorodithioic acids (**FMC 78123**, **FMC 78135** and **FMC 78115**). No single fraction exceeded 8% of the total radioactivity recovered.
Readily biodegradable (yes/no)	Not readily biodegradable
Degradation in water/sediment - DT_{50} water ‡ - DT_{90} water ‡ - DT_{50} whole system ‡ - DT_{90} whole system ‡	2 systems : A (20°C, 1.7%OC) B (20°C, 10.1%OC) Water: DT_{50lab} : A=38, B=36 days DT_{90lab}: A=126, B=121 Whole system: DT_{50lab} : A=59, B=68 DT_{90lab}: A=195, B=226
Mineralization	CO_2: 12 - 18.2 % AR (at 100 d, study end)
Non-extractable residues	6 - 8.3 % AR (at 100 d, study end)
Distribution in water / sediment systems (active substance) ‡	Surface water-sediment extract after 100 days (% AR): A=15-15, B=13.9-20.9
Distribution in water / sediment systems (metabolites) ‡	One minor degradation product was identified as methyl-2-butyl sulfone but accounted for 1% or less in most samples.

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

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

Parent

Method of calculation	DT_{50}: 38 days Representative worst case from sediment water study
Application rate	Crop: potatoes Number of applications: 1 Application rate: 6000 g a.s./ha Depth of water body: 30 cm
Main routes of entry	Spray–drifts of 2.77, 0.57, 0.29, 0.20 0.15 and 0.1% (buffer zones of 1, 5, 10, 15 20 and 30m)

PECsw								
Days After Treatment	DT_{50} = 38 days							
	Actual Con. (µg/L)				Time-weighted Average (µg/L)			
	Buffer zones				Buffer zones			
	1 m	5 m	10 m	15 m	1 m	5 m	10 m	15 m
0	55.40	11.40	5.80	4.00	55.40	11.40	5.80	4.00
1	54.40	11.19	5.69	3.93	54.90	11.30	5.75	3.96
2	53.41	10.99	5.59	3.86	54.40	11.19	5.69	3.93
4	51.50	10.60	5.39	3.72	53.43	10.99	5.59	3.86
7	48.76	10.03	5.10	3.52	52.01	10.70	5.44	3.75
14	42.91	8.83	4.49	3.10	48.89	10.06	5.12	3.53
21	37.77	7.77	3.95	2.73	46.02	9.47	4.82	3.32
28	33.24	8.84	3.48	2.40	43.38	8.92	4.54	3.13
42	25.75	5.30	2.70	1.86	38.70	7.96	4.05	2.79
50	22.25	4.58	2.33	1.61	36.34	7.48	3.80	2.62
100	8.94	1.84	0.94	0.64	25.47	5.24	2.67	1.84

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

PECsw				
Days After Treatment	DT_{50} = 38 days			
	Actual Con. (µg/L)		Time-weighted Average (µg/L)	
	Buffer zones		Buffer zones	
	20 m	30 m	20 m	30 m
0	3.00	2.00	3.00	2.00
1	2.95	1.96	2.97	1.98
2	2.89	1.93	2.95	1.96
4	2.79	1.86	2.89	1.93
7	2.64	1.76	2.82	1.88
14	2.32	1.55	2.65	1.76
21	2.04	1.36	2.49	1.66
28	1.80	1.20	2.35	1.57
42	1.39	0.93	2.10	1.40
50	1.20	0.80	1.97	1.31
100	0.48	0.32	1.38	0.92

Parent

Method of calculation	PRZM runoff modeling for a Tenerife specific scenario
Application rate	Crop: bananas Number of applications: 1 Application rate: 6000 g a.s./ha via drip irrigation Depth of water body: as defined by FOCUS at step 3
Main routes of entry	runoff

In this specific geoclimatic example (Tenerife) no surface runoff was predicted by the PRZM parameterisation (soil infiltration rate was too high). Therefore in Tenerife surface water exposure would be expected to be negligible. It is not appropriate to extrapolate this conclusion to other banana growing locations.

PEC (sediment)

Parent

Method of calculation	23% partitioning to sediment after 59 days, sediment layer of 2 cm, bulk density: 1.3 g/cm^3, pattern of decline reflecting that measured in the sediment/water study

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

Application rate	Crop: potatoes Number of applications: 1 Application rate(s): 6000 g a.s./ha

Distance from application	1 m	5 m	10 m	20 m	30 m
PECsw, max (µg/L)	55.4	11.4	5.8	3	2
PEC sed, (mg/kg)	0.15	0.03	0.014	0.008	0.005

Metabolite

Method of calculation	PRZM runoff modeling for a Tenerife specific scenario
Application rate	Crop: bananas Number of applications: 1 Application rate: 6000 g a.s./ha via drip irrigation sediment: as defined by FOCUS at step 3
Main routes of entry	runoff

In this specific geoclimatic example (Tenerife) no surface runoff was predicted by the PRZM parameterisation (soil infiltration rate was too high). Therefore in Tenerife sediment exposure would be expected to be negligible. It is not appropriate to extrapolate this conclusion to other banana growing locations.

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

Acceptable calculations not available. Data required.

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

Direct photolysis in air ‡	Not submitted, not required
Quantum yield of direct phototransformation	Not relevant due to the low photochemical degradation
Photochemical oxidative degradation in air ‡	DT_{50} of 1.1 hours which corresponds to 0.089 days when a 12-hour day is considered and to 0.045 days when 24-hour day is considered (derived by the Atkinson method of calculation)
Volatilization ‡	from plant surfaces : Not submitted, not required from soil (BBA guideline): 1.13 % of AR after 48 hours

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

PEC (air)

Method of calculation	Expert judgment, based on vapour pressure, information on volatilisation from soil.

$PEC_{(a)}$

Maximum concentration	PEC values in air are expected to be negligible. Therefore, calculation of PECA is not required.

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	The metabolism of cadusafos in soil, water, sediment and air did not show formation of major metabolites. Therefore, only the parent compound is included in soil, surface water, sediment and air residue definition. For groundwater further data on methyl-2-butyl sulfone is required before the residue definition can be concluded.

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

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Candidate for R53

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

Appendix 1.6: Effects on non-target Species

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

Acute toxicity to mammals ‡	LD_{50} 37.1 (32.2-42.0) mg/kg bw (rat) (a.s.)
Long-term toxicity to mammals	NOAEL 0.045 mg/kg b.w./day (rat) (a.s.)
Acute toxicity to birds ‡	LD_{50} 16.1 mg/kg bw/day (Bobwhite quail) (a.s.) LD_{50} 102.6 mg/kg (formulation-Rugby 200CS/Bobwhite quail) (formulation)
Dietary toxicity to birds ‡	LC_{50} 10.8 mg/kg bw/day (42.5 ppm) (Bobwhite quail) (a.s.)
Reproductive toxicity to birds ‡	NOEL ≥1.1 mg/kg bw/day (≥12 ppm) (Bobwhite quail) (a.s.)

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

Application rate (kg a.s./ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
6	Potato/banana	insectivorous bird	Acute	2.58	10
6	potato/banana	insectivorous bird	Short-term	17.3	10
6	potato/banana	insectivorous bird	Long-term	1.76	5
6	Potato(1)	fish eating birds	Long-term	7.2 (15 m)	5
6	potato	earthworm eating birds	Long-term	**0.05**[2]/7.6[3]	5
6	banana	earthworm eating birds	Long-term	**0.009**[2]/1.9[3]	5
6	potato(1)	fish eating mammal	Long-term	**0.95** (30 m)	5
6	potato	earthworm eating mammal	Long-term	**0.002**[2] **/ 0.243**[3]	5
6	banana	earthworm eating mammal	Long-term	**0.003**[2]/0.06[3]	5

(1) Bananas: Just for the specific geoclimatic situation in Tenerife the potential for surface water exposure is considered by the EFSA to be negligible, so the risk to fish eating birds and mammals will be low.
(2) First tier according to SANCO 4245/2000
(3) Based on measured residues in earthworms from laboratory study (artificial soil with high organic content)

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

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
Laboratory tests ‡				
Rainbow Trout (*Salmo gairdneri*)	cadusafos	acute (96 h)	LC_{50}	130
Bluegill sunfish	cadusafos	acute (96 h)	LC_{50}	170
Rainbow Trout (*Salmo gairdneri*)	cadusafos	long-term (95 days)	NOEC	5.22
Daphnia magna	cadusafos	acute 48 h	EC_{50}	0.75
Daphnia magna	cadusafos	long-term 21 d	NOEC	0.231
Scenedesmus subspicatus	cadusafos	acute 72 h acute 24 h	EbC_{50} ErC_{50}	4300 5700
Chironomus riparius	cadusafos	long-term 28 d	NOEC	32 (µg/kg)
Oncorhynchus mykiss	Rugby 200CS	acute (96 h)	LC50	4500
Daphnia magna	Rugby 200CS	acute 48 h	EC50	1.1
Selanastrum capricornumtum	Rugby 200CS	acute 71 h	EbC50 ErC50	21000 48000

Microcosm or mesocosm tests
Lowest NEC (Cladocera) = 0.05 µg/L Recovery from adverse direct effects = 1.25 µg/L Recovery from indirect (stimulation) effects = 0.06 µg/L

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

Application rate (kg a.s./ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
6	potato	fish	acute	1	**2.3**	100
6	potato	fish	acute	30	**65**	100
6	potato	fish	long term	1	**0.1**	10
6	potato	fish	long term	30	**3.1**	10

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

Application rate (kg a.s./ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
6	potato	*Daphnia magna*	acute	1	**0.014**	100
6	potato	*Daphnia magna*	acute	30	**0.375**	100
6	potato	*Daphnia magna*	long term	1	**0.005**	10
6	potato	*Daphnia magna*	long term	30	**0.135**	10
6	potato	*Scenedesmus subspicatus*	acute	1	78	10
6	potato	*Chironomus riparius*	long term	1	**0.168**	10
6	potato	*Chironomus riparius*	long term	30	**4.57**	10
6	potato	zooplancton/ mesocosm	long-term	1	0.001	3 (agreed by EPCO)
6	potato	zooplancton/ mesocosm	long-term	30	0.03	3 (agreed by EPCO)
6	banana	Just for the specific geoclimatic situation in Tenerife the potential for surface water exposure is considered by the EFSA to be negligible, so the risk will be low.				

Bioconcentration

Bioconcentration factor (BCF) ‡	220 (whole fish), 150 (fillet), 260 (viscera).
Annex VI Trigger:for the bioconcentration factor	100
Clearance time (CT_{50}) (CT_{90})	Not reported
Level of residues (%) in organisms after the 14 day depuration phase	70% (whole fish), 61% (fillet), 75% (viscera)

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

Acute oral toxicity ‡	LD_{50} 2.07 µg a.s./bee
Acute contact toxicity ‡	LD_{50} 1.80 µg a.s./bee

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

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

not applicable: direct exposure not expected

Application rate (kg a.s./ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
6	potato/banana*	oral	2899	50
6	potato/banana*	contact	3333	50

*Since application is only to bare soil the risk is considered to be low

Field or semi-field tests
Not required

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

Species	Stage	Test Substance	Dose (kg a.s./ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests ‡						
Aphidius rhopalosiphi		Rugby 200CS	5000	mortality	100	30
Typhlodromus pyri		Rugby 200CS	5000	mortality	100	30
Extended laboratory tests						
Aphidius rhopalosiphi		Rugby 200CS	0.5-8	LR_{50}	3.75 g a.s./ha	
			0.5	mortality	6.7	
			1	mortality fecundity	6.7 20.4 (ns)	
			2	mortality fecundity	6.7 10.2	
			4	mortality	46.7	
			8	mortality	93.3	

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

Species	Stage	Test Substance	Dose (kg a.s./ha)	Endpoint	Effect	Annex VI Trigger
Typhlodromus pyri		Rugby 200CS	1-100	LR_{50}	44.4 g a.s./ha	
			1	mortality	0.0	
			10	mortality fecundity	10.6 5.0	
			20	mortality fecundity	22.8 7.5	
			40	mortality	35.0	
			80	mortality	83.8	
			100	mortality	79.6	

Species	Stage	Test Substance	Dose (kg a.s./ha)	Endpoint	Effect	Annex VI Trigger
semi-field tests						
Poecilus cupreus		Rugby 200CS	4500	mortality 14 d mortality 14-28d	81.8 12.5	30 30

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

Acute toxicity ‡	Rugby 10G LC_{50} 7.2 mg a.s./kg dry wt Rugby 200 CS LC_{50} 12.5 mg a.s./kg dry wt (6.25 mg a.s./kg dry wt corrected)
Reproductive toxicity ‡	Rugby 200 CS NOEC 1.8 mg ai /kg dry wt (0.9 mg a.s./kg dry wt corrected)

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

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

Application rate (kg a.s./ha)	Crop	Time-scale	TER	Annex VI Trigger
6	Potato	acute	**4.8**	10
6	Potato	long term	**0.69**	5
6	Banana	acute	**0.8**	10
6	Banana	long term	**0.11**	5

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

Nitrogen mineralization ‡	No effects up to 50 kg a.s./ha
Carbon mineralization ‡	No effects up to 50 kg a.s./ha

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N; Dangerous to the environment; R50 Very toxic to aquatic organisms; R53 May cause long-term adverse effects in the aquatic environment;

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

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

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