European Food Safety Authority

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CONCLUSION ON PESTICIDE PEER REVIEW

Peer review of the pesticide risk assessment of the active substance cadusafos[1]

(Question No EFSA-Q-2009-00201)

Re-issued on 8 April 2009

SUMMARY

Cadusafos is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[2], as amended by Commission Regulation (EC) No 1490/2002[3]. 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 discussion of the outcome of the consultation of experts following the procedure set out in Commission Regulation (EC) 451/2000 took place with representatives from the Member States on 9 February 2006 leading to the conclusions set out in the EFSA Conclusion issued on 24 April 2006 (EFSA Scientific Report (2006) 68)

Following the Commission Decision of 18 June 2007 (2007/428/EC)[4] concerning the non-inclusion of cadusafos in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the notifier FMC Chemical made a resubmission application for the inclusion of cadusafos in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No.

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

[3] OJ No L 224, 21.08.2002, p. 25

[4] OJ No L160, 21.6.2007, p. 26

33/2008. The resubmission dossier included further data in response to the areas of concern identified in the review report as follows:

- the potential contamination of groundwater
- the operators exposure
- the risk to birds and mammals
- its possible impact on non-target organisms

Greece, being the designated rapporteur Member State, submitted the additional report on cadusafos to the EFSA on 15 October 2008. In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA dispatched the additional report to Member States and the notifier for consultation. The comments received were subsequently submitted to the Commission for evaluation. In accordance with Article 20 of Commission Regulation (EC) No. 33/2008, the Commission subsequently requested the EFSA, by letter received on 8 January 2009, to arrange a peer review of the evaluation, i.e. the additional report provided by the rapporteur Member State, and to deliver its conclusion on the risk assessment within 90 days.

The peer review was initiated on 14 January 2009 by dispatching the comments received on the additional report to the rapporteur Member State for examination. The rapporteur provided a response to the comments in the reporting table, which was subsequently evaluated by EFSA to identify the remaining issues to be further considered in a series of scientific meetings via teleconferences with Member State experts in March 2009.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in March-April 2009. The EFSA conclusion has therefore been re-issued to update the risk assessment in the areas of identity, physical, chemical and technical properties and methods of analysis, mammalian toxicology, residues, environmental fate and behaviour, and ecotoxicology.

The original conclusion from the review was reached on the basis of the evaluation of the representative uses as insecticide and nematicide as presented in the DAR, which comprise application by spraying or via the drip irrigation system to control a range of soil insects and nematodes in potatoes and bananas at application rates of up to 6 kg cadusafos per hectare. In case of potatoes incorporation into soil takes place after the application. 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 conclusion of the peer review of the resubmission was reached on the basis of the evaluation of the representative use as insecticide and nematicide, which comprise application via the drip irrigation system to control a range of soil insects and nematodes in bananas at application rates of up to 4 kg cadusafos per hectare. It should be noted that the use on potatoes was not supported in the resubmission application either, and therefore the conclusion has only been updated in relation to the risk assessment of the representative uses presented in the additional report, i.e. only the use on bananas at application rates of up to 4 kg cadusafos per hectare. The risk assessment presented for potatoes has not been updated.

The representative formulated product for the evaluation was 'Rugby 200 CS', a capsule suspension (CS). Preparations containing cadusafos were registered in Cyprus, France, Greece and Spain.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.
Adequate analytical methods are available to monitor cadusafos in food of plant origin, environmental matrices and body fluids and tissues.

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, there was 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 but not valid. A further assessment of the genotoxic potential of the impurity was required.

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. 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 4 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, with the use of gloves, 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 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, two metabolism studies for this crop were originally submitted, and the data were not sufficient to propose a residue definition. This was 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 was needed, as well as residue trials carried out according to the representative use pattern.

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.

In the resubmission, only the use on banana is supported with a lower application rate of 4 kg as/ha instead of 6 kg as/ha, and a harvest interval of 90 days instead of 14 days. A new plant metabolism study showed that no significant metabolites are formed. None of the minor metabolites formed will have the anticholinesterase activity of cadusafos. The study confirms that the residue definition is cadusafos only. Overdosed residue trials showed that no significant residues will be present at harvest even with shorter harvest intervals. A TMDI calculation using the EFSA model showed that the highest intakes were <5% of the ADI. The acute risk assessment gave intakes at <30 % of the ARfD. The proposed MRL for banana is 0.01* mg/kg. It should be noted however, that cadusafos has two chiral carbons and it is not known if the ratio of the isomers remains the same as the material tested in the mammalian toxicity studies.

The available data demonstrate that in soil cadusafos degrades to the minor (<10% applied radioactivity (AR)) metabolite methyl-2-butyl sulfone[5]. 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, though this categorisation for methyl-2-butyl sulfone is based only a single experimental DT_{50} value.

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 two consecutive sampling points in a soil route of degradation study, data on its mobility in soil are required to enable a groundwater exposure assessment for this metabolite to be carried out.

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

[5] methyl-2-butyl sulfone: (2*RS*)-2-(methylsulfonyl)butane

* MRL proposed at LOQ

not be applied to bananas grown elsewhere. The available aquatic exposure assessment from the use on potatoes is appropriate for addressing just the spray drift route of entry to surface water for initial PEC in aquatic systems. Surface water exposure and consequent aquatic risk assessments from the run-off and drainage routes of entry are not available for the potato use.

The available FOCUS groundwater modelling for bananas in Tenerife for the parent cadusafos and for the metabolite methyl-2-butyl sulfone are not satisfactory, and the potential for groundwater contamination is therefore currently unclear. New groundwater modelling is therefore required for cadusafos and for the soil metabolite methyl-2-butyl sulfone.

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 were not further considered.

For the use in banana plantations a high risk was identified for insectivorous and earthworm-eating birds and mammals in a first-tier risk assessment. The proposed refinement was not accepted by the experts due to the lack of supporting data. However, due to the mode of application (drip-irrigation), only 16% of the in-field area is treated, leaving the majority of food items uncontaminated (the exposure of epigaec insects was considered negligible). This information could be used in a weight of evidence approach for a qualitative risk assessment.

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. For the application of cadusafos by drip irrigation to banana plants no off-field exposure is expected. No new data was provided with the resubmission dossier. No further data was considered necessary for the use in banana plantations, since only 16% of the in-field area is treated leaving enough uncontaminated refuges, which would allow the recolonisation of the treated area.

A high acute and long-term risk was identified for earthworms. The field study conducted in the United Kingdom was considered not appropriate for the risk assessment for banana plantations. A data gap was identified to provide information on the potential for recolonisation of earthworms in the treated area of banana plantations, or alternatively, a study on effects on earthworm populations in banana plantations.

A study with Collembola and mites was required to address the risk to other soil macro-organisms. No study with Collembola was provided with the resubmission dossier. However, the experts considered further data not necessary for banana plantations, since only 16% of the in-field area is treated leaving enough uncontaminated refuges, which would allow the recolonisation of the treated area.

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

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BACKGROUND

Commission Regulation (EC) No 451/2000 laying down the detailed rules for the implementation of the second and third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC, as amended by Commission Regulation (EC) No 1490/2002, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. 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 discussion of the outcome of the consultation of experts following the procedure set out in Commission Regulation (EC) 451/2000 took place with representatives from the Member States on 9 February 2006 leading to the conclusions set out in the EFSA Conclusion issued on 24 April 2006 (EFSA Scientific Report (2006) 68).

Following the Commission Decision of 18 June 2007 (2007/428/EC)[6] concerning the non-inclusion of cadusafos in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the notifier FMC Chemical made a resubmission application for the inclusion of cadusafos in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No 33/2008. The resubmission dossier included further data in response to the areas of concern identified in the review report as follows:

- the potential contamination of groundwater
- the operators exposure
- the risk to birds and mammals
- its possible impact on non-target organisms

[6] OJ No L160, 21.6.2007, p. 26

Greece, being the designated rapporteur Member State, submitted the additional report on cadusafos to the EFSA on 15 October 2008. In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA dispatched the additional report to Member States and the notifier for consultation. The comments received were subsequently submitted to the Commission for evaluation. In accordance with Article 20 of Commission Regulation (EC) No. 33/2008, the Commission subsequently requested the EFSA, by letter received on 8 January 2009, to arrange a peer review of the evaluation, i.e. the additional report provided by the rapporteur Member State, and to deliver its conclusion on the risk assessment within 90 days.

The peer review was initiated on 14 January 2009 by dispatching the comments received on the additional report to the rapporteur Member State for examination. The rapporteur provided a response to the comments in the reporting table, which was subsequently evaluated by the EFSA to identify the remaining issues to be further considered in a series of scientific meetings via teleconferences with Member State experts in March 2009.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in March-April 2009. The EFSA conclusion has therefore been re-issued to update the risk assessment in the areas of identity, physical, chemical and technical properties and methods of analysis, mammalian toxicology, residues, environmental fate and behaviour, and ecotoxicology.

The original conclusion from the review was reached on the basis of the evaluation of the representative uses presented in the DAR, i.e. use as insecticide and nematicide which comprises 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. 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. It should be noted that the use on potatoes was not supported in the resubmission application either, and therefore the conclusion has only been updated in relation to the risk assessment of the representative uses presented in the additional report, i.e. only the use on bananas at application rates of up to 4 kg cadusafos per hectare. The risk assessment presented for potatoes has not been updated.

A list of the relevant end points for the active substance as well as for the formulation is provided in appendix A.

The documentation developed during the resubmission 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 additional report:

- the comments received
- the resulting reporting table (rev. 1-1 of 28 January 2009)

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 8 April 2009).

Given the importance of the additional report including its addendum (compiled version of April 2009) and the peer review report with respect to the examination of the active substance, these documents are considered respectively as background documents A and B to this conclusion. The documents of the peer review report and the final addendum developed during the course of the initial review process are made publicly available as part of the background documentation to the original conclusion, *EFSA Scientific Report* (2006) 68, 1-70, finalised on 24 April 2006.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

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

It should be noted that cadusafos contains two chiral carbon atoms. When finalising the conclusion, the EFSA identified a data gap that the isomeric composition of the active substance should be clarified, and any consequent implications for the risk assessment from the isomers that may be present should be addressed.

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

The representative formulated product for the evaluation was 'Rugby 200 CS', a capsule suspension (CS), containing 200 g/L cadusafos. Preparations containing cadusafos were registered in Cyprus, France, Greece and Spain.

The representative uses evaluated during the original submission comprise applications by spraying (with incorporation into soil after the application) or via the drip irrigation system to control a range of soil insects and nematodes in potatoes and bananas, at a single application, at maximum application rate of 6 kg a.s./ha. It should be noted however, that the use on potatoes is no longer supported by the notifier for Annex I inclusion.

The representative use evaluated during the resubmission comprises application through drip irrigation system to control a range of soil insects and nematodes in bananas, in Canary Islands, at a single application, at maximum application rate of 4 kg a.s./ha.

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. There is no FAO specification available.

The new 5-batch data were evaluated in the Volume 4 of the additional report, and the rapporteur Member State requested the removal of a number of impurities not detected at all from the new specification proposed. The revised proposed specification was presented in Addendum 2 to Volume 4 and accepted by the rapporteur Member State and also by the PRAPeR Expert Meeting Teleconference (PRAPeR TC 08) on mammalian toxicology (March 2009). The PRAPeR TC 06 meeting of experts on physical, chemical and technical properties (March 2009) however did not accept the specification for some impurities, and requested further justification (e.g. QC data) for specifying them or to remove them from the specification. It should also be noted that the PRAPeR TC 09 meeting of ecotoxicological experts (March 2009) set a data gap for information whether the batches used in the ecotoxicological studies cover the specification proposed (see section 5).

Since clarification is required with respect to the proposed maximum levels of certain impurities in the technical material, the specification as a whole should be regarded as provisional for the moment.

The assessment of the data package revealed no other 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:

-information about the purity of one of the starting materials

-information on the shear rate at which the viscosity measurement has been conducted

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

Adequate analytical methods are available for the determination of cadusafos in the technical material and in the representative formulation (GC-FID), as well as for the determination of the respective impurities in the technical material (GC-FID, GC-MS).
Sufficient test methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.
Adequate analytical methods are available to monitor cadusafos in food of plant origin, environmental matrices and body fluids.

Residues of cadusafos in food of plant origin can be monitored by GC-NPD with LOQs of 0.005 mg/kg (bananas, tomatoes). The applicability of a multi-residue method was not tested as it should have been done, therefore a new data gap has been identified by the EFSA.
An analytical method for food of animal origin is not required due to the fact that no MRLs are proposed (see section 3.4).

Residues of cadusafos in soil can be monitored by GC-MS with a LOQ of 0.007 mg/kg. Adequate methods are available to monitor cadusafos residues in drinking water by GC-NPD with a LOQ of 0.1 µg/l, and in surface water by GC-MS with a LOQ of 0.009 µg/l. Cadusafos residues in air can be determined by GC-NPD with a LOQ of 9 ng/m^3.
Residues of cadusafos in body fluids and tissues can be monitored by GC-NPD with LOQs of 0.005 mg/l (urine and blood), and by LC-MS/MS with LOQs of 0.005 mg/kg (meat and liver).

2. Mammalian toxicity

Cadusafos was discussed at EPCO 28 meeting of experts on mammalian toxicology (June 2005). During the resubmission process (Additional Report of October 2008), an additional report was provided by the rapporteur Member State. Based on the comments raised by the Member States, a further experts' meeting took place in March 2009 (PRAPeR Expert Meeting Teleconference 08).

The equivalence of the batches used in the toxicological studies and the new technical specification (January 2009) was discussed by the experts. Their attention focused on two impurities (8 and 17, according to the Additional Report to Annex C - October 2008), which were present in unknown or lower amounts in the tested batch. It was concluded that further assessment of the genotoxic potential of these impurities should be provided in order to demonstrate their (non-)relevance and the acceptability of the proposed levels in the technical specification (see also section 2.8).

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-(2-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 as 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 repeated exposure by inhalation. During the resubmission procedure, the peer-review took into account the low acute inhalation toxicity of the formulation as well as the intended outdoor use by automatic drip irrigation, and it was agreed that no additional repeat-dose study by inhalation was necessary.

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 and carcinogenicity

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 and developmental 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 are 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. This proposal of no classification for teratogenicity was agreed during the ECB meeting of the Technical Committee on Classification and Labelling of Dangerous Substances in 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 major non rat metabolites of cadusafos, 1-carboxy-hydroxyisopropylmethyl sulfone[7] isomers (found in potato tubers) was discussed in the DAR. These metabolites were 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-butylmethyl sulfone[8]). Furthermore, it was stated that they were transient metabolites, likely to be biotransformed *via* decarboxylation to carbon dioxide.

Conclusively, these metabolites were considered of no toxicological concern.

Hydroxy-2-butane sulfonic acid[9] is not a rat metabolite, and no toxicity studies were submitted by the notifier. 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 compound. During the resubmission, it was also considered that this metabolite is a hydroxylated form of a rat metabolite detected up to 7% in urine and faeces. Taking all these points into consideration, the peer review agreed that hydroxy-2-butane sulfonic acid was of low toxicological concern and no additional toxicological data were required.

In a position paper on the potential groundwater metabolite **methyl-2-butyl sulfone**[10], a structural relationship with dimethyl sulfone was used to demonstrate its toxicological non-relevance. This was considered insufficient by the experts. Pending on the confirmation of the groundwater level for this metabolite, further information will have to be provided by the applicant to demonstrate the absence of severe toxicological properties, at least in comparison with the parent compound.

Impurities

As a consequence of a change in the manufacturing process for cadusafos and the introduction of a new impurity (8), 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 rapporteur Member State due to lower numbers 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. During the resubmission, no further data were available for this new batch used in a valid Ames test.

During the PRAPeR Teleconference 08, another impurity (17) was shown to be at lower amount in the batch used for the toxicological studies than in the proposed technical

[7] 1-carboxy-hydroxyisopropylmethyl sulfone: (2*RS*,3*RS*)-2-hydroxy-3-(methylsulfonyl)butanoic acid
[8] hydroxy-2-butylmethyl sulfone: (2*RS*,3*RS*)-3-(methylsulfonyl)butan-2-ol
[9] hydroxy-2-butane sulfonic acid: (2*RS*,3*RS*)-3,4-dihydroxybutane-2-sulfonic acid
[10] methyl-2-butyl sulfone: (2*RS*)-2-(methylsulfonyl)butane

specification (January 2009). Due to the high acute toxicity of cadusafos, the experts agreed that the notifier should address the potential for genotoxicity of these two impurities in order to demonstrate their (non-)relevance and the acceptability of their proposed levels in the technical specification.

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. During the resubmission, it was mentioned that no issues with depressed cholinesterase levels had been identified in workers monitored after possible exposure during the manufacturing process.

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 for the derivation of the reference values.

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**.

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 and the resubmission, the supported uses were limited to treatment of bananas by automatic drip irrigation.

Operator exposure

According to the intended uses submitted by the applicant the maximum applied dose is 4 kg cadusafos/ha diluted in 48,000 L of water/ha.

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 200 CS) after dilution in water has been studied and the results show that 1.12% of the total amount is in solution (free to come in contact with human skin) after 2 minutes (and 4.10% after 4 hours). This value was used to represent a worst case for "free" cadusafos in the concentrate. Nevertheless, no information on the stability of the microcapsules during storage is available.

The operator exposure estimates for a reduced application rate (4 kg instead of 6 kg cadusafos/ha) were already provided in the Addendum 3 (June 2005). According to the German and UK POEM models (only taking into account the exposure during mixing and loading), the estimated operator exposure is below the AOEL with the use of gloves, see table below.

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 UK POEM and 70 kg in German model.

Model	No PPE	With PPE:
German	272	7
UK POEM (5L container)	223	11
UK POEM (20L container)	279	14

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

The standard models used to assess operator exposure are not directly applicable to the scenario under consideration, but were considered to be a worst case. The following 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%

It was noted during the meeting that no information on the stability of the microcapsules was available. That might in theory influence the amount of cadusafos released. It was decided to address this at Member State level.

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 48,000 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.

During the resubmission, it was also considered that the application rate had been lowered (4 instead of 6 kg cadusafos/ha), the post-harvest interval had been increased, and the potential exposure to volatilized pesticide was not considered as a source of concern.

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.

3. Residues

Cadusafos was discussed at the EPCO 29 meeting of experts on residues (July 2005). During the resubmission process (Additional Report of October 2008), an additional report was provided by the rapporteur Member State. There were no comments on this report and peer review in a meeting of experts was not necessary.

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

The metabolism and translocation of cadusafos[11] 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 presented in the DAR on bananas were extensively discussed during the EPCO 29 meeting of experts 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 originally proposed PHI (14 days as proposed by the notifier, or 28 days as alternatively proposed by the rapporteur Member State). Information is therefore was only available for long PHIs, with hydroxy-2-butane sulfonic acid, methyl-2-butyl sulfone and hydroxy-2-butylmethyl sulfone being the main organosoluble degradation products identified in bananas. Unchanged cadusafos was also present in low amounts. No information was 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)-

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

phosphorothioic acid and S-(2-butyl)-phosphorothioic acid) and therefore potentially having cholinesterase inhibition activity, should be carefully investigated.

In the resubmission only the use on banana is supported with a lower application rate at 4 kg as/ha instead of 6 kg as/ha, and a harvest interval of 90 days instead of 14 days. A new plant metabolism study showed that no significant metabolites are formed. None of the minor metabolites formed will have the anticholinesterase activity of cadusafos. The study confirms that the residue definition for all crops is cadusafos only.

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-hydroxyisopropylmethyl sulfone 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 the 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 that 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 end points that have been derived (see section 2.10). The data gap for 4 additional residue trials in potatoes is not supported by the rapporteur Member State, 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, in the original DAR no residues trials reflecting the applied for intended Southern EU use are available from Southern Europe. A data gap was therefore identified.

In the resubmission, 4 new trails on banana conducted in Spain were supplied. Residues at circa 90 days were all less than 0.01 mg/kg. Even with a shorter PHI no residues were detected above 0.01 mg/kg. Given the above and the fact that all the trials were overdosed (6.5 kg as/ha), it can be concluded that the database is sufficient and no further data are required.

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 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

From the data available in the DAR a consumer risk assessment was difficult to conduct, 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 rapporteur Member State.

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, 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.

For the resubmission, only a modified use on banana was supported. A TMDI calculation using the EFSA model showed that the highest intakes were <5% of the ADI. The acute risk assessment gave intakes at <30 % of the ARfD. It should be noted, however, that cadusafos has two chiral carbons and it is not known whether the ratio of the isomers remains the same as the material tested in the mammalian toxicity studies.

3.4. Proposed MRLs

From the data in the DAR there were insufficient residues trials available to propose MRLs for potatoes. However, this expectation would need to be validated, should the results from the residues trials on potato identified as a data gap become available.

For the resubmission an MRL of 0.01* mg/kg for banana is proposed.

* MRL is proposed at LOQ

No MRLs are currently proposed for products of animal origin to due expected very low exposure of domestic animals.

4. Environmental fate and behaviour

Cadusafos was discussed at the EPCO 26 meeting of experts on environmental fate and behaviour (June 2005). The applied for intended use in Southern Europe on potatoes was not critically peer reviewed by the Member States experts at the EPCO meeting, as the applicant had indicated that 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. The comments and observations in this conclusion relating to the use on potatoes therefore originate from the EFSA or the rapporteur Member State only. Following the resubmission application, cadusafos was discussed at the PRAPeR Expert Meeting Teleconference (PRAPeR TC 07) in March 2009 on the basis of the additional report dated October 2008. This additional report only considered a use on bananas.

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

In soil experiments carried out on three 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 two 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 four different soils incubated in the laboratory in the dark at 20 °C and 40% maximum water

holding capacity (MWHC), 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[12], 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 one soil at 25°C the single first-order DT_{50} for cadusafos was 48.6 days. In the aerobic soil incubation, where the metabolite methyl-2-butyl sulfone was present above 5% AR at 2 consecutive time points, a single first-order DT_{50} of 4.5 days (equivalent to 5.3 days at 20 °C and -10kPa moisture content) was estimated for methyl-2-butyl sulfone (kinetic formation fraction 0.315 that is associated with the cadusafos DT_{50} of 12.3 days, see report from PRAPeR Teleconference 07). The Member State experts in PRAPeR Teleconference 07 concluded that aerobic soil DT_{50} for methyl-2-butyl sulfone are necessary in at least two additional soils to complete the environmental exposure assessment. Consequently, they agreed that this should be identified as a data gap in this conclusion.

In field dissipation studies carried out at three 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). It should be noted that 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.

It was agreed as appropriate to calculate predicted environmental concentrations using a single first-order DT_{50} of 59 days (maximum field dissipation study value from trials carried out in Southern Europe. For the use in bananas, as application is made via drip irrigation to individual plants, there will be a spatial element to soil exposure concentrations, with concentrations around the plants (where the drip irrigators are) being higher than the soil in the spaces between the banana plants. The applicant accounted for this by making the following assumptions about the layout of banana plantations, that the Member State experts in PRAPeR Teleconference 07 found reasonable: 'The cadusafos from each dripper spreads in soil to a depth of 15-20 cm. If the horizontal spread through the soil was assumed to equal 20 cm per dripper, then each dripper would treat an area of $0.13m^2$. With six drippers per tree the treated area per tree would be $0.78m^2$. Normal spacing between banana trees in the Canary Islands is 2.0m within rows, and either 2.5m or 3.0m between rows. Taking 2.5m as a worst case, this gives an area occupied by each tree of $5m^2$. The treated soil area per tree ($0.78m^2$) therefore represents 16% of the total area per tree. Expanding this to the whole plantation it can be said that 16% of the soil surface area of a banana plantation would be treated.' The experts agreed that the estimate, that only 16% of the surface area of a banana plantation would result in cadusafos exposure, might be considered reasonable, but noted that in deeper soil layers the spread of the active substance might be greater than at the surface. Even at the soil surface, exposure might exceed the 16% estimate, but it was agreed that there would be some proportion of the surface area with negligible exposure. Of course this 16% estimate depends on the particular plantation layout (distances between trees) stated above, which might be significantly different in locations outside the canaries. The experts noted that using

[12] Generic guidance for FOCUS groundwater scenarios version 1.1 dated April 2002 using a Q10 of 2.2 and Walker equation coefficient of 0.7. The individual values calculated by EFSA were 14.6, 32.3, 38.4, 38.5, 49.7, 55.9 & 62 days.

the 16% assumption, a PEC soil around the treated banana plants would be around 32 mg/kg (assuming the substance remained primarily in the top 5cm soil layer).

4.1.3. Mobility in soil of the active substance and their metabolites, degradation or reaction products

In guideline batch adsorption studies on four 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.

A quantitative structure activity relationship (QSAR) estimated K_{doc} value was provided by the applicant for methyl-2-butyl sulfone in the resubmission. The Member State experts in PRAPeR Teleconference 07 concluded that a study should be required to assess the adsorption of this metabolite, since there was no technical reason or other justification presented why a measured adsorption value had not been provided. The need of a study was considered justified by the experts, because the available estimated groundwater concentrations for methyl-2-butyl sulfone are border line with respect to the 0.1 µg/L parametric drinking water value, and the QSAR estimate is expected to have up to one order of magnitude uncertainty. A data gap is therefore indicated in this conclusion.

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 1.2m). During the experiment the groundwater table was as close to the soil surface as 0.7m. The parent compound cadusafos was determined in these samples of groundwater at a maximum of 0.4 µg/L 270 days after application, decreasing to 0.4 µg/L 1 year after application. (Note, for information, that the 'best fit' soil dissipation DT_{50} determined for cadusafos at this trial site was 46 days (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, contamination of groundwater above the parametric drinking water limit of 0.1 µg/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 of 6 kg/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. 3.5m (0.5m below the average level of the groundwater table of 3m), approximately tri monthly for up to 21 months after the first application. The parent compound 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 that these positive findings in the 45 day samples resulted from contamination via the 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, that the single first-order soil dissipation DT_{50} determined for cadusafos at this trial site was 38 days). 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 run-off 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 run-off 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 in the original submission, but reflecting that requested in the resubmission). This modelling calculated surface water concentrations of <0.001 µg/L and sediment concentrations of <0.001 µg/kg dw. Whilst, when taken at face value, this modelling did not use a high enough application rate to cover the original submission, 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 EPCO meeting of experts were unable to conclude whether 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[13], 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

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

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 run-off 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 run-off and drainage routes of entry will contribute little to surface water exposure, it could be appropriate for this to be addressed by Member States 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 or other FOCUS groundwater scenarios. 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 the DAR dated January 2006). The EPCO meeting of experts were unable to conclude whether 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[14], but is still not available in any addenda to the DAR. The EFSA considered 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} values were estimated using measured residues in all soil layers where residues were detected, the contribution of leaching to deeper soil layers to the DT_{50} 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 considered that it could be appropriate to use field single first-order soil DT_{50} values as input in the leaching modelling, provided that a Henry's law constant of 0 Pa. m^3 mol^{-1} was also used as input, so that volatilisation losses are not double counted.

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

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 been normalised to reference conditions, the corrections for temperature and moisture content in 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 was not in accordance with the applied for intended use at that time of 6kg a.s./ha (applied through drip irrigation systems at a rate of up to 4g per plant).

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[15]. 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 0.1 µg/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.

In the resubmission application, standard FOCUS groundwater simulations using the scenarios defined for citrus were submitted, which the applicant proposed should be used to cover the applied for intended use on bananas at 4 kg a.s./ ha (applied through drip irrigation systems). The Member State experts in PRAPeR Teleconference 07 discussed this modelling approach but considered that it should not be accepted, because the applicant had previously demonstrated that a specific Tenerife scenario (with respect to soil hydrological parameterisation) was needed to cover the leaching risk pertinent to the applied for intended uses on the Canary Islands. The experts also noted that the available surface water exposure assessment is based on a Canary Islands specific parameterisation with high soil infiltration rates that precluded surface run-off (and not general FOCUS surface water scenarios defined for citrus), and therefore it would be inconsistent not to use a parameterisation of the soil hydrology specific to the Canary Islands for the groundwater exposure assessment, that would also include high potential infiltration of precipitation. The PRAPeR TC 07 meeting of experts agreed that the following data gap would be appropriate: Groundwater simulations

[15] 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.

using PEARL and PELMO or PRZM and the FOCUS climate scenario definition for Sevilla in combination with the soil hydrological parameterisation described in the scenario that was outlined in the modelling report 'Jarvis T (2005) Predicted Environmental Concentrations of Cadusafos in Surface Water Following Use on Bananas in the Canary Islands FMC Chemical sprl, Brussels Belgium, Study No: FM22305-1'. Simulations should include application dates that cover all the possible application times for bananas. For cadusafos, if just the available data are utilised, a geomean single first-order laboratory soil DT_{50} (at FOCUS reference conditions normalised using an appropriate Q10 and Walker coefficient of 0.7) and K_{Foc} of 227 mL/g and 1/n= 0.988 should be used as input. Inputs for methyl-2-butyl sulfone should be consequent to the results of the data gaps identified for additional soil adsorption investigations and soil degradation rate data for this metabolite. An appropriate kinetic formation fraction for methyl-2-butyl sulfone from cadusafos should be used (derived in accordance with FOCUS kinetics guidance). In the currently available acceptable study this value is 0.315.

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 capsule suspension (CS) formulation of cadusafos was incorporated into soil over the top 10 cm, measured volatilisation losses accounted for 1.13% 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 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 27 meeting of experts on ecotoxicology (June 2005). The use in Southern Europe on potatoes, originally applied for, was not critically peer reviewed by the Member States experts, as the applicant had indicated that 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 rapporteur Member State only.

Cadusafos was resubmitted and discussed at the PRAPeR Expert Meeting Teleconference (PRAPeR TC 09) in March 2009 on the basis of the additional report from October 2008 and Addendum 1 from January 2009. A subsequent addendum to the additional report was submitted by the rapporteur Member State after the teleconference to address the indentified open points (Addendum 2, March 2009).

The supported use evaluated was as an insecticide/nematicide in banana plantations in Canary Islands, 4 kg a.s./ha, one application per year (spring or autumn) applied by drip irrigation.

Based on this particular mode of application the applicant argued that only 16% of the in-field area is treated (estimation based on 6 drippers per plant and spacing between plants of 2.0m × 2.5m). The Member State experts in PRAPeR Teleconference 07 on environmental fate and behaviour (PRAPeR TC 07, March 2009) considered this assumption reasonable. However, it was pointed out that the exposure of the local treated area could be about six times higher than the standard estimated PEC_{soil} assuming uniform application (see section 4.1.2).

The present conclusion addresses the risk to non-target organisms, taking into account the particular mode of application (drip irrigation). No conclusion can be drawn on other forms of banana planting and mode of application.

A data gap was identified at the PRAPeR Teleconference 09 for the applicant to provide information whether the batches used in the ecotoxicological studies cover the specification given on page 4 of Addendum 2 to Volume 4.

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 were submitted by the applicant late in the evaluation process of the original peer review, and was therefore not evaluated by the rapporteur Member State nor peer reviewed. Hence, a conclusion on the risk to birds in banana plantations could not be reached at that stage.

As cadusafos has a log Pow >3, and therefore a potential to bioaccumulate, the risk from 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. For the use in potatoes incorporation into a 30cm soil layer was used to calculate the PEC_{soil}. 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.

In the resubmission, a new risk assessment was submitted for small insectivorous birds and insectivorous mammals, and earthworm-eating birds and mammals in banana plantations.

Small insectivorous birds and insectivorous mammals

Due to the mode of application, to calculate the TER values, the rapporteur Member State assumed that the residues in soil arthropods is equal to the PEC_{soil} (i.e. RUD = 5.33). Since cadusafos is highly toxic, no accumulation in insects is expected, therefore the Member State experts agreed to use the PEC_{soil} as a surrogate for residues in insects. According to the

conclusion of the PRAPeR TC 07 meeting of experts on environmental fate and behaviour, that on 16% of the in-field treated area the PEC_{soil} may be six times higher, the PRAPeR TC 09 meeting of experts agreed to use a rough estimate of PEC_{soil} by multiplying by six the current PEC_{soil} of 5.33 mg/kg. New TER values were provided by the rapporteur Member State in Addendum 2. For insectivorous birds the TER_a is 0.48, the TER_{st} is 0.32 and the TER_{lt} is 0.03. For mammals the TER_a is 1.84 and the TER_{lt} is 0.002.

The rapporteur Member State proposed in Addendum 1 an alternative risk assessment based on RUD values for soil insects of 1 mg/kg (90^{th}) for the acute risk, and 0.1 mg/kg (mean) for the short-term and long-term risk, according to Fletcher *et al*. (1994) (Appendix II of SANCO4145). However, these values were considered more appropriate for substances applied as spray, and not for cadusafos applied as drip irrigation.

Earthworm-eating birds and mammals

The TER values provided by the rapporteur Member State were calculated on the basis of measured residue level in earthworms, derived form a reproduction study with technical cadusafos reported in the original DAR (B.9.6.2). However, these calculations were not agreed by the PRAPeR TC 09 meeting of experts. Measured residues may be used to calculate a BCF, but in this case, since the plateau concentration in earthworms was not reached in the study, a reliable BCF could not be derived. Furthermore, it was noted that the local soil concentration may be higher. Therefore, it was suggested to calculate the first-tier TER based on the standard approach (PEC_{soil}, K_{ow}, K_{oc}).

New TER values of 0.002 and of 0.00006 were calculated by the rapporteur Member State for earthworm-eating birds and mammals, respectively, and provided in Addendum 2.

Risk refinement – Focal species

A refined risk assessment for birds and mammals was provided by the rapporteur Member State (additional report and Addendum 1), based on a literature survey and re-analysis of monitoring data (Giessing B., 2005). In addition to the assumptions used in the first-tier risk assessment (i.e. PEC_{soil} as RUD for insects and measured residues as RUD for earthworms), already discussed above, focal species were proposed to address the risk to insectivorous and earthworm-eating birds and mammals, as well as refined PD and PT values.

Birds

As focal species for birds, the rapporteur Member State suggested to use the blackbird (*Turdus merula*), a predominantly vermivorous/omnivorous bird. The Member State experts agreed, but it was noted from the Giessing B. (2005) report that small insectivorous birds like grey wagtail (*Motacilla cinerea*) occur in banana plantations. Therefore, the PRAPeR TC 09 meeting of experts considered necessary to address the risk also for this guild (data gap).

For blackbird a mixed diet (PD) was proposed (66% epigaec arthropods and gastropods, 6% endogaec arthropods, 22% earthworms). The proposed PD values were not agreed by the experts, since they were not supported by data, which would allow to justify such quantitative refinements. Therefore, a data gap was identified to provide studies supporting the suggested PD values. In this context, it should be underlined that the PRAPeR TC 09 meeting of experts considered the residues on epigaec arthropods negligible due to the mode of application of cadusafos in banana plantations.

PT values of 0.82 (95^{th}) and 0.218 (50^{th}) extrapolated from a field study conducted in the United Kingdom (Crocker *et al*., 1998) were proposed for the acute and long-term risk refinement, respectively. The PRAPeR TC 09 experts considered the extrapolation from

orchards in the UK to banana plantations uncertain. Therefore, a data gap was identified to provide a scientifically sound argumentation. However, it was agreed to use the 95th PT for the long-term risk assessment (instead of the 50th), and not to use any PT refinements for acute risk assessment. The resulting TER_{lt} of 0.04 was provided in Addendum 2.

Mammals

As focal species for mammals, Algerian hedgehog (*Atelerix algirus*) was proposed. However, the key literature studies were not provided with the dossier, therefore it was not possible for the rapporteur Member State and the experts to verify the suggested focal species. A data gap was identified to provide such studies. Furthermore, the PRAPeR TC 09 meeting of experts noted that also smaller mammals were listed in the Giessing B. (2005) report, like Osorio shrew (*Crocidura Osorio*), which may not be excluded in banana plantations on Gran Canaria. In this case the risk for Algerian hedgehog would not cover the risk to shrew since the latter is much smaller (data gap).

For Algerian hedgehog a mixed diet (PD) was proposed (66% epigaec arthropods and gastropods, 6% endogaec arthropods, 13% earthworms, 4% others). As for birds, the proposed PD values were not agreed, since they were not supported by data. Therefore, a data gap was identified to provide such information. In this context, it should be underlined that the PRAPeR TC 09 meeting of experts considered the residues on epigaec arthropods negligible due to the mode of application of cadusafos in banana plantations.

The experts discussed the proposed PT value of 0.3, which was considered by the applicant and the rapporteur Member State as worst-case, based on the assumption that Algerian hedgehog does prefer shrub-like vegetated areas, and it is unlikely that it forages exclusively in banana plantations on a long-term time-scale. However, without supporting data, the experts considered the use of qualitative data in a quantitative way as not acceptable. Therefore, a data gap was identified to provide data supporting this PT refinement.

The experts discussed the relevance of reproductive effects of cadusafos on mammals. The original NOAEL of 0.045 mg/kg bw/day, based on behavioural effects (reduced locomotion in females), was considered as a conservative value. The experts agreed that some refinement based on maternal toxicity may be possible, if information on the reversibility of the behavioural effects would be available. Therefore no new end point was suggested.

Overall, it could be concluded that the first-tier TER values indicated a high risk for insectivorous and earthworm-eating birds and mammals. Most of the proposed options for refinement were rejected by the PRAPeR TC 09 experts because of lack of supporting data, and several data gaps were identified (to address the risk for small insectivorous birds and mammals; to provide data to justify the proposed focal species; to provide data to support the PD and PT refinement). Therefore, on the basis of available data, it was not possible to exclude a high risk for birds and mammals in the treated area of banana plantations. However, it should be taken into account that only 16% of the in-field area is treated due to the drip irrigation, which would leave the majority of feed items uncontaminated. For the same reason the exposure to epigaec insects was considered negligible. The PRAPeR TC 09 meeting of experts agreed that this information could be used in a weight of evidence approach for a qualitative risk assessment.

The risk to fish-eating birds and mammals was assessed 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 30cm deep water body at 1m distance. For fish-eating birds 15m buffer zones would be required to meet the Annex VI trigger for the use in potatoes. For mammals the TER value

with a 30m 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 30cm deep water body at different distances from the field. The obtained values are below the Annex VI trigger with a buffer zone of 30m, 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 end point 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 end point 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 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. Mortality at 14 days was 82%, decreasing to 12.5% at days 14-28. 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 20m buffer zones are required to protect non-target arthropods off-field. Since an off-field risk was identified for the potato use, further studies with a second appropriate species are required. This could be addressed with the ongoing study with *Aleochara bilineata*. The EPCO meeting of experts 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*.

No new data were provided with the resubmission. The test with *P. cupreus* conducted at 4.5 kg a.s /ha indicated that toxic effects are short-lived, and that no unacceptable effects must be expected in the field. Moreover, the PRAPeR TC 09 experts agreed to the argumentation that only 16% of the surface is treated in banana plantations, leaving enough uncontaminated refuges, from where recolonisation of the treated area could take place. Therefore the data gap to provide study with *A. bilineata*, identified in the EPCO meeting in 2005, was considered not relevant any longer for banana plantations.

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, based on PEC_{soil} of 5.33 mg/kg multiplied by 6, are 0.2 and 0.03 for acute and long term, respectively, in banana, which are clearly below the Annex VI triggers, 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 30cm soil. The meeting of experts agreed that the ongoing field study conducted in the 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 was below the proposed application rate for the intended uses in the original submission.

The field study conducted in the United Kingdom was provided and peer reviewed. The PRAPeR TC 09 experts noted that no significant effects were observed in this study with the positive control (carbendazim). This questions the validity of the study itself. The soil conditions in the study site in the UK and the exposure conditions (uniform distribution of the active substance in soil instead of points with high concentrations and untreated areas in between) were not comparable to the use in bananas. Cadusafos is not persistent in soil (DT_{50} = 12 – 59 days) and the experts recognised that the degradation of cadusafos under cooler UK weather conditions may be slower compared to the Canary Islands, leading to a longer exposure period. However, the exposure to earthworms could be significantly higher in the treated area of banana plantations (about 6 times the current PEC_{soil}), and since the acute

toxicity to earthworms is high, this would lead to a high mortality, locally. Due to a large area left untreated (84%), and considering that cadusafos is applied only once per year, there could be a potential for recolonisation of the treated part of the field from the untreated parts. However, no data were provided to show that recolonisation is possible, and a potential high risk was not excluded in the treated parts of the field.

Overall, the study was considered not appropriate for the risk assessment. A data gap was identified to provide information on the potential for recolonisation of earthworms in the treated area of banana plantations, or alternatively, a study on effects on earthworm populations in banana plantations.

No major metabolites were detected in the soil degradation studies.

5.6. Risk to other soil non-target macro-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 EPCO meeting of experts agreed that a study with Collembola and mites is required to address the risk. No major metabolites were detected in the soil degradation studies.

No new data was provided with the resubmission. The PRAPeR TC 09 experts agreed to the argumentation that only 16% of the surface is treated in banana plantations, leaving enough uncontaminated refuges, from where recolonisation of the treated area could take place. Therefore, the data gap to provide study with Collembola, identified in the EPCO meeting in 2005, was considered not relevant any more for banana plantations.

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 meeting of experts agreed that no further data are needed. However, for the use on potato 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

6.1. Soil

Definition for risk assessment:	cadusafos
Definition for monitoring:	cadusafos

6.2. Water

6.2.1. Ground water

Definition for exposure assessment:	cadusafos and methyl-2-butyl sulfone
Definition for monitoring:	cadusafos. Currently further fate and behaviour data are required before it can be concluded if methyl-2-butyl sulfone would also need to be included in a monitoring definition.

6.2.2. Surface water

Definition for risk assessment	
in surface water:	cadusafos
in sediment:	cadusafos
Definition for monitoring:	cadusafos

6.3. Air

Definition for risk assessment:	cadusafos
Definition for monitoring:	cadusafos

6.4. Food of plant origin

Definition for risk assessment:	cadusafos
Definition for monitoring:	cadusafos

6.5. Food of animal origin

Definition 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.
Definition for monitoring:	The same as ‘definition for risk assessment’ above.

6.6. Body fluids and tissues

Definition for monitoring:	cadusafos

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

6.7.1. 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

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

6.7.3. Surface water and sediment

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

6.7.4. 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

- Clarification on the isomeric composition of the active substance and an assessment of any consequent implications for the risk assessment from the isomers that may be present (relevant for all representative uses evaluated, data gap identified by EFSA when finalising the conclusion, date of submission unknown; refer to chapter 1)
- A revised specification for the technical material or justification (e.g. QC data) for the proposed levels of some impurities (relevant for all representative uses evaluated, data gap identified by PRAPeR TC 06 meeting of experts (March 2009), date of submission unknown; refer to chapter 1)
- Information on the purity of one of the starting materials (relevant for all representative uses evaluated, data gap identified by PRAPeR TC 06 meeting of experts (March 2009), date of submission unknown; refer to chapter 1)
- Information on the shear rate at which the viscosity measurement has been conducted (relevant for all representative uses evaluated, data gap identified by the evaluation meeting and confirmed by the EPCO 30 meeting of experts (July 2005) and PRAPeR TC 06 meeting of experts (March 2009), date of submission unknown; refer to chapter 1)
- The applicability of a multi-residue method for the determination of residues of cadusafos in food of plant origin (relevant for all representative uses evaluated, data gap identified by EFSA when finalising the conclusion, date of submission unknown; refer to chapter 1)
- Applicant to assess the genotoxic potential of the two impurities (8) and (17) in order to demonstrate their (non-)relevance and the acceptability of the proposed levels in the technical specification (relevant for all representative uses evaluated, data gap identified by PRAPeR TC 08 meeting of experts (March 09), date of submission unknown; refer to point 2.8)
- Pending on the confirmation of the level of the metabolite methyl-2-butyl sulfone in the groundwater (see below), further information on its toxicological relevance should be provided by the applicant (data gap identified by PRAPeR TC 08 meeting of experts, refer to point 2.8)
- Applicant to submit further 4 residues trials data that support the use in potatoes in Southern Europe, analysing for cadusafos with an LOQ of 0.005 mg/kg (data gap agreed at the meeting of experts; refer to point 3.1.1.; this data gap is for information only as it refers to the non-supported use; the data gap becomes relevant only, should this use be considered again in the future).
- 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 (relevant for the use in potatoes in Southern Europe; data gap identified in the DAR and confirmed at the meeting of experts; refer to point 3.1.2; this data gap is for information only as it refers to the non-supported use; the data gap becomes relevant only, should this use be considered again in the future).

- Aerobic soil DT_{50} are required for methyl-2-butyl sulfone in at least 2 additional soils (relevant for all representative uses evaluated; data gap identified by the PRAPeR TC 07 meeting of experts, date of submission unknown, refer to point 4.1.2).
- A guideline batch adsorption study investigating adsorption of methyl-2-butyl sulfone in at least 3 different soils (relevant for all representative uses evaluated; data gap identified by the PRAPeR TC 07 meeting of experts, date of submission unknown, refer to point 4.1.3).
- PEC surface water and sediment from the potato use addressing the drainage and run-off routes of entry to surface water and a consequent aquatic risk assessment (relevant for the Southern European potato use evaluated; data gap identified by EFSA; refer to point 4.2.1; this data gap is for information only as it refers to the non-supported use; the data gap becomes relevant only, should this use be considered again in the future)
- FOCUS groundwater modelling using PEARL and PELMO or PRZM for the potato use utilising appropriate cadusafos soil degradation and volatilisation input parameters. Inputs for methyl-2-butyl sulfone to be consequent to the results of the data gaps identified for additional soil adsorption investigations and soil degradation rate data for this metabolite. An appropriate kinetic formation fraction for methyl-2-butyl sulfone from cadusafos should be used (derived in accordance with FOCUS kinetics guidance). In the currently available acceptable study this value is 0.315 (relevant for the Southern European potato use evaluated; data gap identified by the expert meetings; refer to point 4.2.2; this data gap is for information only as it refers to the non-supported use; the data gap becomes relevant only, should this use be considered again in the future).
- Groundwater simulations using PEARL and PELMO or PRZM and the FOCUS climate scenario definition for Sevilla in combination with the soil hydrological parameterisation described in the scenario that was outlined in the modelling report 'Jarvis T (2005) Predicted Environmental Concentrations of Cadusafos in Surface Water Following Use on Bananas in the Canary Islands FMC Chemical sprl, Brussels Belgium, Study No: FM22305-1'. Simulations to include application dates that cover all the possible application times for bananas. For cadusafos, if just the available data are utilised, a geomean single first-order laboratory soil DT_{50} (at FOCUS reference conditions normalised using an appropriate Q10 and Walker coefficient of 0.7) and K_{Foc} of 227mL/g and 1/n= 0.988 should be used as input. Inputs for methyl-2-butyl sulfone to be consequent to the results of the data gaps identified for additional soil adsorption investigations and soil degradation rate data for this metabolite. An appropriate kinetic formation fraction for methyl-2-butyl sulfone from cadusafos should be used (derived in accordance with FOCUS kinetics guidance). In the currently available acceptable study this value is 0.315 (relevant for the banana use evaluated; data gap identified by the PRAPeR TC 07 meeting of experts, date of submission unknown, refer to point 4.2.2).
- The applicant should provide information whether the batches used in the ecotoxicological studies cover the specification given on page 4 of Addendum 2 to Volume 4 (data gap identified by the PRAPeR TC 09 meeting of experts, date of submission unknown, refer to section 5).
- The risk to birds and mammals should be addressed for the potato use (the applicant has indicated that use on potato is no longer supported therefore it was not discussed during the peer review) (data gap agreed in the EPCO meeting; refer to point 5.1; this data gap

is for information only as it refers to the non-supported use; the data gap becomes relevant only, should this use be considered again in the future)

- Data to support the proposed focal species (blackbird (*Turdus merula*)), PD and PT refinements to address the risk to birds in banana plantations should be provided (data gap identified by the PRAPeR TC 09 meeting of experts, relevant for banana plantations in Canary Islands; refer to point 5.1)
- Data to support the proposed focal species (Algerian hedgehog (*Atelerix algirus*)), PD and PT refinements to address the risk to mammals in banana plantations should be provided (data gap identified by the PRAPeR TC 09 meeting of experts, relevant for banana plantations in Canary Islands; refer to point 5.1)
- Risk to small insectivorous birds and small insectivorous mammals in banana plantations should be addressed (data gap identified by the PRAPeR TC 09 meeting of experts, relevant for banana plantations in Canary Islands; refer to point 5.1)
- The risk to fish should be further addressed (relevant for the use in potatoes; refer to point 5.2; this data gap is for information only as it refers to the non-supported use; the data gap becomes relevant only, should this use be considered again in the future).
- The risk to aquatic invertebrates should be further addressed (relevant for the use in potatoes; refer to point 5.2; this data gap is for information only as it refers to the non-supported use; the data gap becomes relevant only, should this use be considered again in the future).
- The risk to non-target arthropods should be further addressed in order to show the potential for in-field recolonisation and recovery (data gap agreed in the EPCO meeting; relevant for the use in potatoes; refer to point 5.4; this data gap is for information only as it refers to the non-supported use; the data gap becomes relevant only, should this use be considered again in the future).
- Data on the potential for recolonisation of earthworms in the treated area of banana plantations, or alternatively, a study on effects on earthworm populations in banana plantations should be provided (data gap identified by the PRAPeR TC 09 meeting of experts, relevant for banana plantations in Canary Islands; 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 the EPCO meeting; relevant for the use in potatoes; refer to point 5.6; this data gap is for information only as it refers to the non-supported use; the data gap becomes relevant only, should this use be considered again in the future).
- A study on effects on non-target flora is required (relevant for the use in potatoes; refer to point 5.8; this data gap is for information only as it refers to the non-supported use; the data gap becomes relevant only, should this use be considered again in the future).

CONCLUSIONS AND RECOMMENDATIONS

OVERALL CONCLUSIONS

The original conclusion from the review was reached on the basis of the evaluation of the representative uses as an insecticide and nematicide as presented in the DAR, which comprise application by spraying or via the drip irrigation system to control a range of soil insects and nematodes in potatoes and bananas at application rates of up to 6 kg cadusafos per hectare. In case of potatoes incorporation into soil takes place after the application. 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 conclusion of the peer review of the resubmission was reached on the basis of the evaluation of the representative use as insecticide and nematicide, which comprise application via the drip irrigation system to control a range of soil insects and nematodes in bananas at application rates of up to 4 kg cadusafos per hectare.

The representative formulated product for the evaluation was "Rugby 200 CS", a capsule suspension (CS). Preparations containing cadusafos were registered in Cyprus, France, Greece and Spain.

Since clarification is required with respect to the proposed maximum levels of certain impurities in the technical material, the specification is still provisional.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection products are possible.
Adequate analytical methods are available to monitor cadusafos in food of plant origin, environmental matrices and body fluids and tissues. An analytical method for food of animal origin is not required due to the fact that no MRLs are proposed.

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, there was 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 but not valid. A further assessment of the genotoxic potential of the impurity was required.

The ADI is 0.0004 mg/kg bw/day, the AOEL is 0.0007 mg/kg bw/day, and the ARfD is 0.003 mg/kg bw. 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 4 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, with the use of gloves, 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 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, two metabolism studies for this crop were originally submitted, however, the data were not sufficient to propose a residue definition. This was 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 was needed as well as residue trials carried out according to the representative use pattern.

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.

In the resubmission, only the use on banana is supported with a lower application rate of 4 kg as/ha instead of 6 kg as/ha, and a harvest interval of 90 days instead of 14 days. A new plant metabolism study showed that no significant metabolites are formed. None of the minor metabolites formed will have the anticholinesterase activity of cadusafos. The study confirms that the residue definition is cadusafos only. Overdosed residue trials showed that no significant residues will be present at harvest even with shorter harvest intervals. A TMDI calculation using the EFSA model showed that the highest intakes were <5% of the ADI. The acute risk assessment gave intakes at <30 % of the ARfD. The proposed MRL for banana is 0.01* mg/kg. It should be noted, however, that cadusafos has two chiral carbons and it is not known whether the ratio of the isomers remains the same as the material tested in the mammalian toxicity studies.

The experimental data available on the fate and behaviour in the environment is generally sufficient to carry out an appropriate environmental exposure assessment at EU level for cadusafos, however experimental data are missing for the metabolite methyl-2-butyl sulfone. In addition, the provision of several acceptable exposure assessments is outstanding. For the use on potato the drainage and run-off routes of exposure to surface water have not been covered for cadusafos in the available EU level assessment. For the applied for intended uses

on both potato in southern 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 these groundwater assessments. 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, therefore it should not be used to support authorisations on bananas in other locations.

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 were not further considered.

For the use in banana plantations, a high risk was identified for insectivorous and earthworm-eating birds and mammals in a first-tier risk assessment. The proposed refinement was not accepted by the experts due to the lack of supporting data. However, due to the mode of application (drip irrigation), only 16% of the in-field area is treated, leaving the majority of food items uncontaminated (the exposure of epigaec insects was considered negligible). This information could be used in a weight of evidence approach for a qualitative risk assessment.

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. For the application of cadusafos by drip irrigation to banana plants no off-field exposure is expected. No new data was provided with the resubmission dossier. No further data was considered necessary for the use in banana plantations, since only 16% of the in-field area is treated, leaving enough uncontaminated refuges which allow the recolonisation of the treated area.

A high acute and long-term risk was identified for earthworms. The field study conducted in the United Kingdom was considered of not appropriate for the risk assessment in banana plantations. A data gap was identified to provide information on the potential for recolonisation of earthworms in the treated area of banana plantations, or alternatively, a study on effects on earthworm populations in banana plantations.

A study with Collembola and mites was required to address the risk to other soil macro-organisms. No study with Collembola was provided with the resubmission dossier. However, the experts considered further data not necessary for banana plantations, since only 16% of the in-field area is treated leaving enough uncontaminated refuges, which would allow the recolonisation of the treated area.

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.

Particular conditions proposed to be taken into account to manage the risk(s) identified (for the use on bananas supported in the resubmission)

- Use of gloves by operators during mixing and loading.
- Not more than 16% of the in-field area should be treated (6 drippers per plant and spacing between plants of 2.0m × 2.5m)

CRITICAL AREAS OF CONCERN
(for the use on bananas supported in the resubmission)

- The specification cannot be finalised, because the relevance of two impurities should be clarified as well as the maximum levels of certain impurities in the technical material (refer to chapter 1 and 2)
- 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.
- A potential high risk for insectivorous and earthworm-eating birds and mammals was identified in a first-tier assessment in the 16% of the in-field area. Additional information was considered necessary to support the proposed refinements (i.e. focal species, PD and PT). Moreover, the suggested focal species did not cover the risk for small insectivorous birds and mammals.
- A high acute and long-term risk to earthworms was indicated in the first-tier assessment. The field study conducted in the United Kingdom was considered not suitable to address the risk in banana plantations and further data were required to demonstrate the potential for recolonisation.

APPENDICES

APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

Changes as a result of resubmission evaluation highlighted in yellow

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

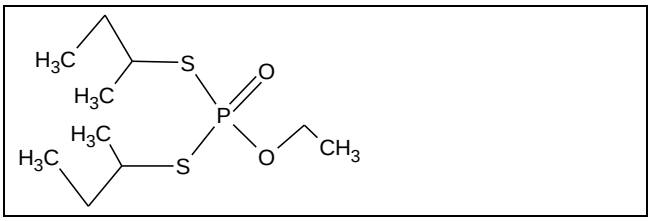
Active substance (ISO Common Name) ‡	Cadusafos
Function (*e.g.* fungicide)	Insecticide and nematicide

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
EC No (EINECS or ELINCS) ‡	Not available
FAO Specification (including year of publication) ‡	Not available
Minimum purity of the active substance as manufactured ‡	900 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Open
Molecular formula ‡	$C_{10}H_{23}O_2PS_2$
Molecular mass ‡	270.4 g/mol

Structural formula ‡



Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	No solidification was observed; Freezing point < - 65 ^{o}C (pure 98.1%)
Boiling point (state purity) ‡	114-115 ^{o}C at 107 Pa (pure 98.1%)
Temperature of decomposition (state purity)	Not determined
Appearance (state purity) ‡	pure a.s. (98.1%): clear colourless liquid at room temperature technical a.s. (91.9%): yellow liquid at room temperature
Vapour pressure (state temperature, state purity) ‡	1.196 x 10^{-1} Pa at 25^{o}C (technical 94.2%)
Henry's law constant ‡	1.32 x 10^{-1} Pa m^{3} mol^{-1} at 25^{o}C
Solubility in water (state temperature, state purity and pH) ‡	245 mg/L at 25 ^{o}C (pure 98.1%) pH was not reported; it was stated that pH was neutral.
Solubility in organic solvents ‡ (state temperature, state purity)	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)
Surface tension ‡ (state concentration and temperature, state purity)	42.2 mN/m at 20^{o}C and concentration 197 mg/L (technical 90.9%) 43.3 mN/m at 25^{o}C and concentration 184 mg/L (pure 98.1%)
Partition co-efficient ‡ (state temperature, pH and purity)	log K_{ow} = 3.85 at 20.5 C, in distilled water (pH 5.5) (technical 90.9%)
Dissociation constant (state purity) ‡	Not relevant given the chemical structure.

UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	In neutral medium (CH_3OH): λ_{max} (nm) ε ($Lxmole^{-1}\times cm^{-1}$) 224 884 No significant absorbance at or above 290 nm.
Flammability ‡ (state purity)	Not highly flammable (technical 90.9%) Self-ignition temperature: 270°C (technical 90.9%)
Explosive properties ‡ (state purity)	Non- explosive (technical 90.9%)
Oxidising properties ‡ (state purity)	Cadusafos is not expected to have oxidizing properties (expert's statement)

Summary of representative uses evaluated (cadusafos)[*]

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	Canary Islands	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	0.008	48000	2 g a.s./ mat (plant) ie 4 kg a.s./ha	90	(2)

[*] Uses for which the risk assessment cannot be concluded are marked grey.

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
	(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

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

Technical as (analytical technique)	-GC/FID
Impurities in technical as (analytical technique)	-GC/FID, GC-MS -Karl Fischer's titration method
Plant protection product (analytical technique)	-GC-FID

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Cadusafos
Food of animal origin		No residue definition/no MRL is proposed
Soil[1)]		Cadusafos
Water	surface	Cadusafos
	drinking/ground	Cadusafos
Air		Cadusafos
Body fluids and tissues		Cadusafos

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	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 for bananas and tomatoes Method can be used for enforcement purposes ILV data were provided

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 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/m3
Body fluids and tissues (principle of method and LOQ)	Std No. A-17-00-47: Substrates: human urine, human blood Extraction: Extraction with saturated sodium chloride solution. Partitioning with dichloromethane. Clean-up: SPE Analysis: GC/NPD Determined analyte: cadusafos LOQ: 0.005 mg/L for urine and blood A confirmatory GC-MS method was submitted. Std No. FMC-0701V: Substrates: meat and liver Extraction: Extraction according to module E1 of the multi residue method L00.00-34 (i.e. DFG S19 extended revision) Clean-up: gel permeation chromatograph (module GPC of of the multi residue method L00.00-34) Analysis: LC-MS/MS Determined analyte: cadusafos LOQ: 0.005 mg/kg for meat and liver

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

	RMS/peer review proposal
Active substance	RMS proposal: None

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	Rapid and 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 ($^{14}CO2$) (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)	Cadusafos
Toxicologically relevant compounds ‡ (environment)	Cadusafos

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	30.1 mg/kg bw, females	T; R25
Rabbit LD_{50} dermal ‡	10.7 mg/kg bw, females	T+; R27
Rat LC_{50} inhalation ‡	0.026 mg/l air, females	T+; R26
Skin irritation ‡	Non irritant	
Eye irritation ‡	Non irritant	
Skin sensitisation ‡	Non sensitizer (Buehler)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Decreased RBC cholinesterase activity
Relevant oral NOAEL ‡	0.067 mg/kg bw/day (90-day, rat) 0.02 mg/kg bw/day (1-yr dog, highest dose tested)
Relevant dermal NOAEL ‡	**No data available - not required**
Relevant inhalation NOAEL ‡	**No data available – not required**

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 (female rats) Renal necrotizing arteritis (male mice)
Relevant NOAEL ‡	0.045 mg/kg bw/day (2-yr rat) 0.072 mg/kg bw/day (18-m mouse)
Carcinogenicity ‡	Cadusafos is unlikely to pose a risk to humans

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	No reproductive toxicity effects. No adverse effect in the offspring. Parents: decreased body weight gain (F1) and RBC cholinesterase activity (F0 & F1) at 0.262 mg/kg bw/day (rat)
Relevant reproductive NOAEL	0.371 mg/kg bw/day (rat, highest dose tested)
Relevant parental NOAEL	0.026 mg/kg bw/day (rat)
Relevant offspring NOAEL	0.371 mg/kg bw/day (rat, highest dose tested)

Developmental toxicity

Developmental target / critical effect ‡	Maternal: clinical signs (rat, rabbit), decreased body weight gain (rat) Foetal: decreased body weight (rat), decreased number of live fetuses (rabbit) at maternal toxic doses. No teratogenic effect observed.
Relevant maternal NOAEL ‡	Rat: 6 mg/kg bw/day Rabbit: 0.3 mg/kg bw/day
Relevant developmental NOAEL	Rat: 6 mg/kg bw/day Rabbit: 0.3 mg/kg bw/day

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 (LOAEL = 20 mg/kg bw)
Delayed neurotoxicity ‡	No evidence of delayed neuropathy, NOAEL = 8.0 mg/kg bw/day

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No data - not required
Studies performed on metabolites or impurities ‡	Acute oral toxicity of cadusafos containing the new impurity 8: 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)

According to Notifier's statement: "*To date there have been no issues with depressed cholinesterase levels at none of the facilities where Rugby products are formulated*". No further data were submitted.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.0004 mg/kg bw/day	2-yr rat	100
AOEL ‡	0.0007 mg/kg bw/day	90-d rat	100
ArfD ‡	0.003 mg/kg bw	Developmental study rabbit	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)**

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 4 kg a.i./ha and the following requirements : - use of gloves - automatic drip irrigation - treated area : 1 ha/day No PPE / PPE German: 272 / 7% of AOEL UK POEM, 5L 223 / 11% of AOEL UK POEM, 20L 279 / 14% of AOEL *It has been assumed that a maximum of 1.12% of the a.s. contained in the undiluted product is released from the capsule and can potentially come into contact with the operator's skin.
Workers	Expected exposure levels lower than the AOEL.
Bystanders	Expected 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

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)) Bananas and Tomatoes (Fruits (F))
Rotational crops	None
Plant residue definition for monitoring	Cadusafos (for plants)
Plant residue definition for risk assessment	Cadusafos (for plants)
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 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 for potatoes only. For bananas, this issue is not relevant.

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	

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	4X<0.01*mg/kg		0.01* mg/kg	0.01* mg/kg

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

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 Contribution of bananas: 4.5% of ADI (PRIMO Model, WHO Cluster Diet F)
TMDI (National Diet) (% ADI)	Contribution of potatoes: 13 – 28% of the ADI for infants, toddlers and children in the United Kingdom and in Germany Contribution of bananas: 4.5% of ADI for Swedish general population (PRIMO Model)
Factors included in NEDI	Not relevant
ARfD	0.003 mg/kg b.w./day
Acute exposure (% ARfD)	Potatoes 50 and 35 27.9% of ARfD for infants and toddlers respectively based on UK consumption data Bananas: 27.9% of ARfD for infants based on UK consumption data

Note: the calculations provided here above are to be considered as preliminary for potatoes only 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	0.01* mg/kg

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)	Methyl 2-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, 40%MWHC, aerobic): 50.9, 51.6, 62.1 & 62.3 d (n= 4, r^2 = >0.87), DT_{50lab} (25°C, 75%FC, aerobic): 12.3, 47.1 & 52.2d (r^2 = >0.87) For FOCUS modeling, cadusafos: geometric mean and median DT_{50lab} 38 d[16] (normalisation to pF2, 20°C, aerobic, first-order kinetics); For future FOCUS modeling, cadusafos: geometric mean and median DT_{50lab} 39.6 d[17] and 41.5 d respectively (normalisation to pF2, 20°C, aerobic, first-order kinetics); No specific effect noticed upon soil types. Methyl 2-butyl sulfone DT_{50lab} (25°C, 75%FC, aerobic): 4.5 days associated kinetic formation fraction from cadusafos 0.315 For FOCUS modeling, 5.3 d[1] (normalisation to pF2, 20°C, aerobic, first-order kinetics); For future FOCUS modeling, 5.7 d[2] (normalisation to pF2, 20°C, aerobic, first-order kinetics). Data gap identified for aerobic soil DT_{50} in at least 2 additional soils.
	Parent DT_{90lab} (20°C, aerobic): 169.1, 171.4, 206.3 & 206.8 d (r^2 = >0.87) DT_{90lab} (25°C, aerobic): 41.0, 156.5 & 173.3 d (r^2 = >0.87)
	$DT_{50lab(extrapol)}$ (10°C, aerobic): 40.5- 171.4 d (n= 8), ($DT_{50\ (10°C)} = DT_{50(20°C)} * Q_{10} = DT_{50(20°C)} * 2.2$)

[16] Normalisation assuming a Walker equation coefficient of 0.7 and a Q10 of 2.2.
[17] Normalisation assuming a Walker equation coefficient of 0.7 and a Q10 of 2.58.

	$DT_{50lab(extrapol)}$ (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, 46 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 144mL/g, 1/n 0.97; 200mL/g, 1/n 0.99; 213mL/g, 1/n 1.0; 351mL/g, 1/n 0.99 (arithmetic mean 227mL/g)
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. Methyl 2-butyl sulfone Data gap identified for adsorption measurements from at least 3 soils.

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: 0.05m (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).*

Application rate	Crop: Banana % Plant interception: Banana: Pre-emergence, drip irrigation Number of applications: 1 Interval (d): Not relevant Application rate(s): 4000 g a.s./ha banana

Crop: Banana, Application dose: 4000 g a.s./ha, Inc. depth: 0.05 m

Days after application	Actual Con. (mg/kg)	Time weighted average Con. (mg/kg)
0	5.333	5.333
1	5.271	5.302
2	5.209	5.271
4	5.089	5.210
7	4.912	5.120
14	4.524	4.918
21	4.167	4.726
28	3.838	4.545
42	3.256	4.210
50	2.964	4.033
100	1.647	3.137

NOTE: concentration in soil next to the drip irrigation system will be six times higher than the ones presented in the table, i.e. 32mg/kg.

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

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				
2d	1.28	1.29		
	1.27	1.28		
4d	1.24	1.27		
Long term 7d				
21d				
28d	1.19	1.24		
	1.01	1.15		
50d	0.93	1.10		
	0.72	0.98		
100d	0.40	0.76		

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	2 systems : A (20°C, 1.7%OC) B (20°C, 10.1%OC)
- DT_{50} water ‡	Water: DT_{50lab} : A=38, B=36 days
- DT_{90} water ‡	DT_{90lab}: A=126, B=121
	Whole system:
- DT_{50} whole system ‡	DT_{50lab} : A=59, B=68
- DT_{90} whole system ‡	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.

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

Parent

Method of calculation	PRZM runoff modeling for a Tenerife specific scenario

Application rate	Crop: bananas Number of applications: 1 Application rate: 4000 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 (either water and consequently also solute) was predicted by the PRZM parameterisation (soil infiltration rate of precipitation 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.

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) Run-off and drainage not assessed.

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

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

PEC (sediment)

Parent

Method of calculation	PRZM runoff modeling for a Tenerife specific scenario
Application rate	Crop: bananas Number of applications: 1 Application rate: 4000 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 run-off (either water and consequently also solute) was predicted by the PRZM parameterisation (soil infiltration rate of precipitation 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.

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
Application rate	Crop: potatoes Number of applications: 1 Application rate(s): 6000 g a.s./ha
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) Run-off and drainage not assessed.

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

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

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 PEC_{air} is not required.

Definition of the Residue (Annex IIA, point 7.3)

Environmental occurring residues requiring further assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.	Soil: cadusafos Groundwater: cadusafos and methyl-2-butyl sulfone Surface water: cadusafos Sediment: cadusafos Air: cadusafos

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

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

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
First tier					
4	bananas	Insectivorous bird	Acute**	0.48	10
4	bananas	Insectivorous bird	Short term**	0.32	10
4	bananas	Insectivorous bird	Long term**	0.03	5
4	bananas	Earthworm eating birds	Long term **	0.002	5
4	bananas	Insectivorous mammals	Acute**	1.84	10
4	bananas	Insectivorous mammals	Long term**	0.002	5
4	bananas	Earthworm eating mammal	Long term**	0.00006	5
6	Potato	insectivorous bird	Acute	2.58	10
6	potato	insectivorous bird	Short-term	17.3	10
6	potato	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	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
Higher tier					
4	bananas	Insectivorous bird (focal species blackbird)	Acute**	0.47	10

4	bananas	Insectivorous bird (focal species blackbird)	Short term**	0.32	10
4	bananas	Insectivorous bird (focal species blackbird, PT =0.82)	Long term**	0.04*	5

***** The PT refinement was based on UK data (95th)

****** PEC soil refers to 16% of the area will be treated (standard PECsoil of 5.33 multiplied by 6)

[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)

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 (µg/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)	LC_{50}	4500
Daphnia magna	Rugby 200CS	acute 48 h	EC_{50}	1.1
Selanastrum capricornumtum	Rugby 200CS	acute 71 h	EbC_{50} ErC_{50}	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 = 0.08 µg/L

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

Note these PECsw for potato only account for the spray drift route of entry of cadusafos into surface water. PEC that include runoff or drainage inputs were not available.

Application rate (kg as/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
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)
4	Banana	Just for the specific geoclimatic situation in Tenerife the potential for surface water exposure is considered 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.i./bee
Acute contact toxicity	LD_{50} 1.80 µg a.i./bee

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

not applicable: direct exposure not expected

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
6	potato	oral	2899	50
6	potato	contact	3333	50
Field or semi-field tests Not required				

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

Species	Stage	Test Substance	Dose (g as/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 ai/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	

Typhlodromus pyri		Rugby 200CS	1-100	LR_{50}	44.4 g ai/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	

Field or semi-field tests						
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 ai/kg dry wt Rugby 200 CS LC_{50} 12.5 mg ai/kg dry wt (6.25 mg ai/kg dry wt corrected)
Reproductive toxicity	Rugby 200 CS NOEC 1.8 mg ai /kg dry wt (0.9 mg ai/kg dry wt corrected)

Field tests

A filed test has been conducted in UK at bare soil.

A single application of cadusafos at a rate of 4.5 kg ha^{-1} had no effect on earthworm abundance or biomass in an arable field by the end of the study, approximately one year after application. The exposure of earthworms will be significantly

higher in the treated area (about 6 times higher than the current PECsoil) but this PEC soil refers to 16% of the area that will be treated.

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

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
4	banana	acute	**0.2**	10
4	banana	long term	**0.03**	10
6	Potato	acute	4.8	10
6	Potato	long term	0.69	5

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

Nitrogen mineralization	No effects up to 50 kg as/ha
Carbon mineralization	No effects up to 50 kg as/ha

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N; R50/53

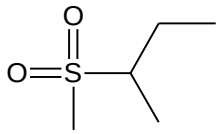
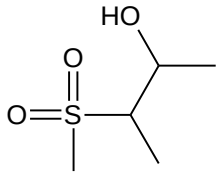
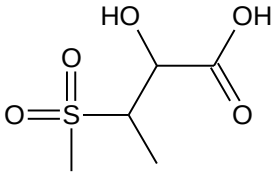
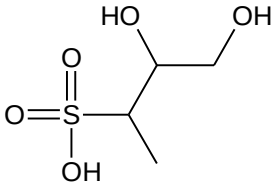
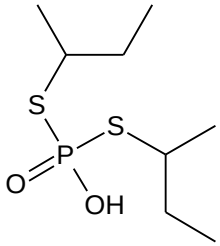
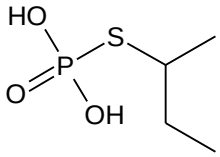
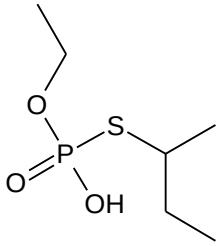
APPENDIX B – LIST OF ABBREVIATIONS

AChE	acetylcholinesterase
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
a.s.	active substance
BCF	bioconcentration factor
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
CHO	Chinese Hamster Ovary
CS	capsule suspension
d	day
DAR	draft assessment report
DM	dry matter
DNA	deoxyribonucleic acid
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
dw	dry weight
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
ECB	European Chemical Bureau
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
FC	field capacity
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)
GC-FID	gas chromatography with flame ionisation detector
GC-MS	gas chromatography-mass spectrometry
GC-NPD	gas chromatography with nitrogen phosphorous detector
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre

HPLC	high pressure liquid chromatography or high performance liquid chromatography
HQ	hazard quotient
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
K_{doc}	organic carbon linear adsorption coefficient
K_{Foc}	Freundlich 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
MWHC	maximum water holding capacity
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
PD	proportion of different food types
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
QC	quality control
QSAR	quantitative structure-activity relationship

r^2	coefficient of determination
RBC	red blood cell
RUD	residue per unit dose
RPE	respiratory protective equipment
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
SC	suspension concentrate
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TWA	time weighted average
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
wk	week
yr	year

APPENDIX C – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name	Structural formula
methyl-2-butyl sulfone	(2*RS*)-2-(methylsulfonyl)butane (2*RS*)-butan-2-yl methyl sulfone	
hydroxy-2-butylmethyl sulfone	(2*RS*,3*RS*)-3-(methylsulfonyl)butan-2-ol	
1-carboxy-hydroxyisopropylmethyl sulfone	(2*RS*,3*RS*)-2-hydroxy-3-(methylsulfonyl)butanoic acid	
hydroxy-2-butane sulfonic acid 2-butane sulfonic acid	(2*RS*,3*RS*)-3,4-dihydroxybutane-2-sulfonic acid	
FMC 78115 *S*,*S*-di(2-butyl)-phosphorothioic acid	*S*,*S*-(2*RS*)-dibutan-2-yl hydrogen phosphorodithioate	
FMC 78123 *S*-(2-butyl)-phosphorothioic acid	*S*-[(2*RS*)-butan-2-yl] dihydrogen phosphorothioate	
FMC 78135	(*RS*)-[*S*-[(2*RS*)-butan-2-yl] *S*-ethyl hydrogen phosphorodithioate]	

- The metabolite name in bold is the name used in the conclusion.