CADUSAFOS (174)

First draft prepared by Dr W Donovan, United States Environmental Protection Agency, Washington DC, USA

EXPLANATION

Cadusafos is an organophosphate nematicide. It was evaluated by JMPR in 1991(T, R) and 1992(R). It was evaluated for toxicological review by JMPR in 2009 as the periodic re-evaluation. The ADI for cadusafos was established as 0–0.0005 mg/kg bw and acute reference dose was 0.001 mg/kg bw

Cadusafos was scheduled at the Forty-first Session of the CCPR (2009) for the periodic re-evaluation of residues by the 2010 JMPR.

Residue studies were submitted by the manufacturer to support the use of cadusafos in or on banana and potatoes.

IDENTITY

ISO common name: Cadusafos

IUPAC name: S,S,-di-*sec*-butyl *O*-ethyl phosphorodithioate

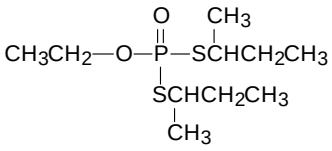
Chemical Abstract name: O-ethyl S,S-bis (1-methylpropyl) phosphorodithioate

CAS No.: 95465-99-9

CIPAC No.: 8042

Molecular Formula: $C_{10}H_{23}O_2PS_2$

Structural Formula:



Molecular Weight: 270.4 g/mol

PHYSICAL AND CHEMICAL PROPERTIES

Pure Active Ingredient (except as noted)

Physical-Chemical Property	Test material purity and specification	Results	Reference
Appearance	Pure Technical	Clear, colourless liquid Clear, yellow liquid	02, Alvarez, 2001
Melting point		< -65 °C	02, Alvarez, 2001
Boiling point		114-115 ºC	02, Alvarez, 2001
Relative Density		1.052 g/ml at 25 °C	02, Alvarez, 2001
Vapour pressure		Extrapolated: 0.1196 Pa for 25 °C	04, Hu, 1984

Physical-Chemical Property	Test material purity and specification	Results	Reference
Thermal Decomposition	Technical	Thermal decomposition was observed at 208 °C	05. Kikta, 2007
Photolysis		DT_{50} = 174 days [deionized water] DT_{50} = 115 days [with 1% acetone as photosensitiser]	06, Tullman, 1988
Solubility of purified active substance in water		245 mg/kg at 25 °C	02, Alvarez, 2001
Solubility in organic solvents	Technical	[g/kg at 25 °C] n-heptane : 125 o-xylene: miscible acetone: miscible ethylacetate: miscible 1,2-dichloroethane: miscible Methanol: > 250	02, Alvarez, 2001
n-Octanol/water partition coefficient		log Kow 3.92 at 25 °C	03, Heckert, 1984
Hydrolysis rate at pH 5, 7 and 9		pH 5 & 7: cadusafos stable The experimental half-life of the test substance at pH 9 was 179 days (25 °C)	07, Witkonton, 1986

FORMULATIONS

A granular test material was used in all banana and potato field trials, except for the potato processing studies where a CS formulation was employed. The registrant provided the following list of cadusafos formulations.

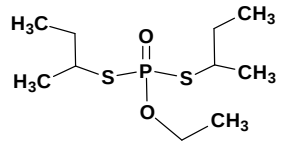
Formulation Type	Active Ingredient Content
GR	30 g/kg
GR	100 g/kg
ME*	100 g/L
CS**	200 g/L

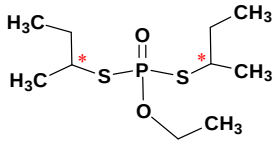
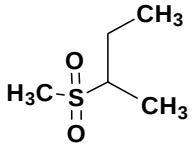
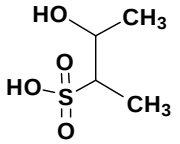
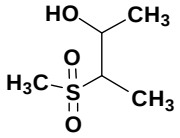
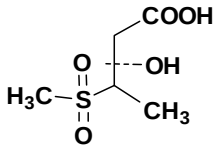
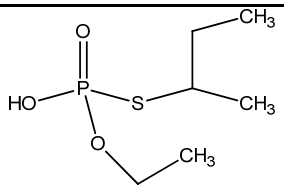
*Microencapsulated Emulsion

** Capsule Suspension

METABOLISM AND ENVIRONMENTAL FATE

Below are presented the structures and identification labels used for compounds found in the plant and rat metabolism studies. Likewise, Figure 1 presents a combined metabolic profile based on the results of these studies.

FMC Number *(Common Name)*	Chemical Name	Structure
FMC 67825 (Cadusafos)	O-Ethyl-S,S-di-sec-butyl phosphorodithioate	

[^{14}C]FMC 67825 ([^{14}C]Cadusafos)	O-Ethyl-S,S-di-2([^{14}C]-butyl phosphorodithioate	
FMC 78121	Methyl-2-butyl sulfone	
FMC 111868	3-hydroxybutane-2-sulfonic acid	
FMC 107620	Methyl-1-methyl-2-hydroxypropane sulfone	
M2 and M3	1 –carboxyhydroxyisopropylmethylsulfone	
FMC 78115 (OSPA)	O-ethyl-S-(2-butyl) phosphorothioic acid	

A proposed metabolic pathway in animals is as follows:

[0]	Oxidation
[CH_3]	Biochemical methylation
P	Pathway proposed in plants
M	Pathway proposed in mammals (rats)

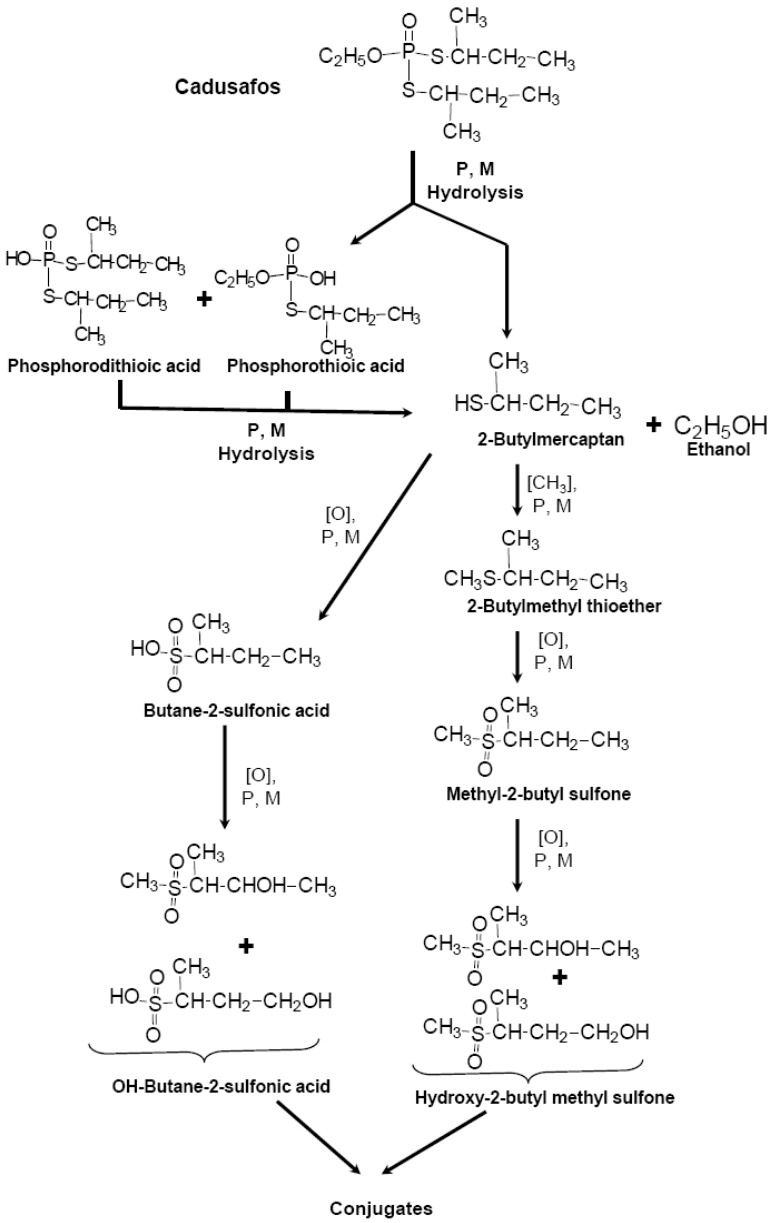


Figure 1 Metabolic Profile of Cadusafos In Plants and Rats.

Animal Metabolism

Three rat metabolism studies were submitted, depicting tissue distribution and metabolite identification following cadusafos dosing of rats by oral and intravenous routes. The Meeting received no poultry or ruminant nature of the residue studies for cadusafos.

Metabolism, distribution and expression of residues in Rats

Radiolabelled cadusafos was administered to Sprague Dawley rats as a single oral dose of 20 mg/kg body weight by gavage (09, Selim, 1984). Excretion of urine, faeces, and $^{14}CO_2$ were monitored for 7 days at which time the rats were sacrificed and blood samples and various tissue/organs were collected and analysed. Excretion of the dosed radioactivity is given in Table 1, which demonstrates that cadusafos is primarily eliminated via the urine and that similar amounts are eliminated in the faeces and expired air. Radioactivity remaining in the tissues ranged from 1.7–2.1% in males and from 1.3–2.9% in females. The highest levels of radioactive residues were found in fat (1.3 mg/kg) and liver samples (0.8 mg/kg).

Table 1 Excretion of dosed radioactivity

Sex	Urine (%)	Faeces (%)	Expired air (%)
Males	74.7 ± 5.3	15.3 ± 2.0	13.4 ± 0.9
Females	78.6 ± 6.5	14.8 ± 8.7	13.7 ± 1.4

A second rat metabolism study was conducted to examine the effect of the following treatment regimens: single oral low dose [SOLD] (1 mg/kg), intravenous dose [IVD] (0.8 mg/kg), and multiple oral low doses [MOLD] (14 doses of unlabelled cadusafos plus one dose of labelled cadusafos, all at 1 mg/kg) (08, Puhl, 1987). The majority of the radioactivity was found in the urine (67.1%, 84.6%, and 71.4%), the faeces (10.1%, 4.9%, and 6.6%), and the CO_2 traps (13.0%, 16.2%, and 15.6%) in the respective groups. Over 90% of the administered dose was eliminated within 48 hours. In rat tissues, the highest residues were found in the liver (up to 0.067 mg/kg) of animals receiving oral doses, and in the lung (up to 0.055 mg/kg) of animals receiving intravenous doses.

A third rat metabolism study was performed in order to identify the metabolites formed in rats following the three dosing regimens in the 1987 study plus a singe oral high dose [SOHD] of 21 mg/kg of labelled cadusafos (10, Wu, 1988). Thus, four groups of 10 male and 10 female Sprague Dawley (CD) rats were treated as follows:

- Single oral low dose (SOLD): 1 mg/kg (^{14}C-test material);
- Single oral high dose (SOHD): 21 mg/kg (^{14}C-test material);
- Single intravenous dose (IV): 0.8 mg/kg (^{14}C-test material);

Multiple oral low dose (MOLD): 1 mg/kg daily for 14 days (non-radiolabelled test material), then on day 15, single oral dose of 1 mg/kg (^{14}C-test material).

Ten animals (5/sex) in each group were transferred to individual stainless steel metabolism cages designed for separation and collection of urine and faeces (168-hour collection after treatment). The remaining 10 rats were transferred to glass metabolism chambers for collection of $^{14}CO_2$ (72-hour collection). Seven days after dosing, the rats were sacrificed, blood samples and various tissue/organs were collected. Animals used for collection of CO_2 were sacrificed 3 days after dosing; no tissue samples were taken from these animals.

Analysis of metabolic degradates by HPLC, TLC, GC/MS, ^{1}H-NMR and liquid scintillation counting showed the presence of parent chemical and 10 identifiable metabolites. The majority of

these products were eliminated in urine (62.65% to 78.88%), faeces (variable according to the dose regimen from 3.81 to 15.26%), and $^{14}CO_2$ (moderate in all dose groups (10.88% to 16.79%) within the first 24 hours after dose. The amount of the administered dose left in the tissue and organs was low (< 0.5%). Carcass showed slightly higher ^{14}C-residues (0.96-2.02%). Quantities of metabolites varied slightly with dose regimen, sex and route of administration.

This study demonstrated that FMC 67825 is readily absorbed, metabolised and eliminated following administration to rats. The majority of administered dose was eliminated in urine, faeces and as expired CO_2 in the first 24 hours after dosing. Hydroxysulfones were detected as the major metabolites followed by phosphorothioic acids, and sulfonic acids. Some of the administered parent compound was excreted in faeces except in intravenously dosed rats. Minor variations were observed between sex and dose but not in significant quantity.

Rat Metabolism Summary

The three submitted rat metabolism studies demonstrated that cadusafos is mainly metabolised by cleavage of the thio-(*sec*-butyl) group, forming two main metabolites: *Sec*-butyl mercaptan and O-ethyl-S-(2-butyl) phosphorothioic acid (OSPA). The latter metabolite is then degraded to S-(2-butyl) phosphorothioic acid or O-ethyl phosphorothioic acid S-(2-butyl). *Sec*-butyl mercaptan produces methyl *sec*-butyl sulfide, sulfoxide, sulfone and hydroxysulfones. The oxidation of *sec*-butyl mercaptan may also produce butyl sulfonic acid, and then, ethyl and methyl sulfonic acid. CO_2 formation may proceed from *sec*-butyl mercaptan or form sulfonic acid. Carbon dioxide is incorporated into urea or other endogenous substances.

Plant metabolism

The Meeting received metabolism studies with cadusafos on the following plants: banana, potato, corn, radish, and tomato. Cadusafos metabolism was relatively consistent in these matrices: oxidation followed by conjugation with glucose took place at several sites of the cadusafos compound. The primary difference noted between plants was the extent of metabolism observed, with potato demonstrating the most extensive metabolism.

Nature of the Residue in Banana

Two banana trees in the early fruiting stage were treated with ^{14}C-cadusafos at the rate of 3.0 g ai. per tree applied to the soil (14, A.A. Ramsey, 1989). Two additional trees were maintained as untreated controls. Mature fruits and leaves from all trees were harvested and processed.

Initial combustion analysis indicated only low levels of total radioactive residue (TRR) in the fruit, 0.051 mg/kg, cadusafos equivalent or lower. Extraction and partition analysis of radiocarbon residue in ripe banana pulp and peel shows that the majority of the residue consisted of water-soluble polar metabolites (52–67%, 0.016–0.035 mg/kg, cadusafos equivalent) while only a lower level of organo-soluble metabolites was found (12–35%, 0.006–0.011 mg/kg, cadusafos equivalent). No parent chemical was detected in the ripe or non-ripe fruit (i.e., < 1 ppb), whereas 1 ppb of parent chemical was found in the leaf. The major metabolites in the ripe pulp and peel appear to be conjugates of transformation products from the 2-butylthio moiety. The transformation products appear to arise from hydroxylation of the thioalkyl chain as well as methylation and/or oxidation of the sulphur atom following hydrolysis of the intact parent organophosphate. Conjugates were cleaved by acid hydrolysis to give compounds identified by chromatography as hydroxy-2-butyl methyl sulfone and hydroxylated butyl-2-sulfonic acid.

In green bananas significantly less (16–21%) of the TRR was present as these polar metabolites, while significantly more (39–55%) of the TRR was identified as methyl 2-butyl sulfone. In addition significant levels of non-extractable residues (25–45% TRR) were seen in the green fruit but these levels had dropped to 15–20 % TRR in the ripe fruit. Table 2 summarises the distribution of cadusafos metabolites found in the banana metabolism study.

Table 2 Distribution of Cadusafos Metabolites in Banana in mg/kg (%)

Tissue	Total Residue	FMC 111868	FMC 107620	FMC 78121	Unextractable	Unassigned
Ripe Pulp	0.051	0.006 (18%)	0.027 (52%)	0.002 (3%)	0.011 (20%)	0.003 (6%)
Ripe Peel	0.031	0.003 (9%)	0.016 (52%)	0.006 (19%)	0.004 (13%)	0.001 (5%)
Non-ripe Pulp	0.031	0.001 (4%)	0.004 (12%)	0.011 (36%)	0.014 (45%)	0.001 (3%)
Non-ripe Peel	0.038	0.001 (3%)	0.007 (18%)	0.018 (48%)	0.009 (25%)	0.002 (5%)
Leaf	0.021	0.002 (9%)	0.006 (30%)	0.004 (19%)	0.003 (14%)	0.003 (15%)

Extensive metabolism of cadusafos occurs in bananas. The predominant residue identified in green banana was FMC 78121 (methyl-2-butyl-sulfone). As bananas ripen to yellow, an additional oxidation step occurs to result in FMC 107620 (methyl-sec-butylhydroxy sulfone) being the predominate metabolite observed.

Nature of the Residue in Potato

Radiolabelled cadusafos was applied onto soils at a rate equivalent to 6 kg ai/ha (16, P. Sabournin, 2002). The majority of metabolite residues present in potato tubers were present in polar and polar conjugated forms. HPLC analysis demonstrated that three major peaks (M1, M2 and M3) accounted for 48.3 and 47.6% (0.331 and 0.332 mg/kg) of the TRR in duplicate samples, respectively. Parent and metabolites present in the organo-soluble CH_2Cl_2 fractions were very minor and constituted a relatively small percentage of the TRR (7.2 and 8.5%, 0.049 and 0.059 mg/kg). Bound residues amounted to 9.8 and 10.6% (0.067 and 0.074 mg/kg) of TRR and were present as carbohydrate incorporated radiocarbon (^{14}C), indicating incorporation into natural products.

M1 was shown by ion-exchange chromatography to consist of a number of polar components each representing less than 0.05 mg/kg (10 %TRR) cadusafos equivalents. Acid hydrolysis of the major aqueous conjugated metabolites (M2 and M3) resulted in releasing their corresponding aglycones. Mass spectral analysis of the acid-released exocons from the polar conjugated metabolites M2 and M3, showed the presence of a single major polar metabolite that existed in two isomeric forms that was characterised/identified as 1-carboxy-hydroxyisopropymethylsulfone.

Since potato tubers represent a storage organ for potato plants and are formed at or after the fully-grown vegetative system has been developed/established, cadusafos related residues most likely go through extensive metabolism in the vegetative shoot system (1st and 2nd phase metabolism to polar conjugates) prior to translocation to the tubers. Previous cadusafos plant and animal metabolism studies showed that the parent compound undergoes hydrolysis to give ethanol, phosphoric acid, and the transient butane-2-thiol. The butane-2-thiol is then quickly either methylated or oxidized to 2-butyl methyl thioether or butane-2-sulfonic acid, both of which undergo extensive metabolic oxidation. In a series of metabolic oxidations associated with conjugation, the 2-butyl methyl thioether can undergo extensive oxidation to its corresponding 2-butyl-methylsulfoxide, 2-butyl-methylsulfone, and hydroxy-2-butyl-methylsulfone all of which are highly polar degradation products. In potato, the hydroxy-2-butyl-methylsulfone that was found as the major rat urinary metabolite and as a major crop residue, was further oxidized to its corresponding carboxylic acid namely 1-carboxyhydroxyisopropylmethylsulfone. Table 3 displays the quantitative identification of cadusafos metabolites found in the potato metabolism study.

Table 3. HPLC Quantitation of ^{14}C–Cadusafos Residue in Treated Potato Tuber Extracts

Component	Potato Tuber 1		Potato Tuber 2	
	%TRR	mg/kg	%TRR	mg/kg
Concentrated Aqueous : Methanol Fraction	66.4	0.455	72.7	0.506
M1	11.2	0.077	16.0	0.112
M2	10.6	0.072	16.1	0.112
M3	26.5	0.182	15.5	0.108

Component	Potato Tuber 1		Potato Tuber 2	
	%TRR	mg/kg	%TRR	mg/kg
Multiple minor peaks	15.0	0.103	17.3	0.121
Concentrated Methylene Chloride Fraction	2.6	0.018	3.9	0.027
~7 Min HPLC Peak	0.7	0.004	1.3	0.009
Cadusafos	0.9	0.006	1.7	0.012
Multiple minor peaks	0.4	0.003	0.7	0.005
PES Fraction	9.8	0.067	10.6	0.074

In summary, cadusafos appeared to undergo extensive metabolism in the potato plant with a portion of the molecule being completely metabolized and incorporated into natural products. Cadusafos undergoes initial hydrolysis to the transient butane-2-thiol, which undergoes a series of oxidations and methylations to yield a major product, hydroxyl-2-butyl-methylsulfone. This compound is further oxidized to two isomers of 1-carboxyhydroxyisopropylmethylsulfone, which, in conjugated form, represent the major metabolites in potato tuber.

Nature of the Residue in Corn

Metabolism of cadusafos was studied in corn using a 2 kg ai./ha treatment regime (11, S.F. El Naggar, 1986). The chemical was applied as a 20% granular formulation in 17.5 cm bands. Corn plants were grown to maturity in the greenhouse. Plant samples were taken at 30 and 60 day post-treatment, at silage, and finally at maturity (i.e., grain and stover). Tissue commodities were initially analysed for total radioactive residues (TRR) and levels of parent chemical. In addition, initial efforts were made to characterise the nature of metabolic plant residues.

Detectable levels of radiocarbon residues were found in corn plants and grain harvested from a 2 kg ai./ha (banded) treatment with ^{14}C cadusafos. Total ^{14}C residues in immature (30, 60 days post plant) and silage samples amounted to 1.54, 0.85 and 0.87 mg/kg (cadusafos equivalents), respectively. Radioactive residues in stover and grain amounted to 2.87 and 0.23 mg/kg, respectively, at 160 days post plant). Extraction/ partition experiments showed that 12–29% of the radioactivity was organosoluble, 40–74% water soluble and 9 –48% bound to plant solids. Parent cadusafos was present only in the 30 day immature plant (forage samples at 7.3% TRR). No parent chemical was detected in grain, stover, silage or 60 day samples. TLC analyses of organosoluble fractions from various harvest intervals showed at least 9 different metabolites.

Cadusafos and/or its metabolites are absorbed and translocated into corn plants following soil application of the parent chemical. Measureable levels of radioactive residues result. However, cadusafos is not stable in the plant and is degraded to more polar and water soluble metabolites.

From the findings in the 1986 corn metabolism study TRR levels ranged from 0.85 mg/kg (cadusafos equivalents) in 60 day post plant forage to 2.87 mg/kg in stover. Grain TRR levels were 0.23 mg/kg cadusafos equivalents found only in the mature (160 day) plant. A new study was conducted to identify polar and bound residues as well as minor products contained in organosoluble fractions of the 1986 study (12, S.F. El Naggar, 1988).

Extraction/partition results indicated substantial quantities of water-soluble polar residues as well as radiocarbon bound to plant solids. Confirmation of individual metabolites was done through direct chromatographic, and co-chromatographic comparison with known standards. In certain cases GC/MS was also employed.

Extraction and partition analysis of radiocarbon residue showed that the majority of the residue consisted of water soluble polar metabolites (0.085–2.021 mg/kg) while a minor level was organosoluble (0.003–0.419 mg/kg). Analysis of the water-soluble polar metabolites from 30 day, 60 day, silage, and stover samples, showed the major metabolic degrades to be 2-butanesulfonic acid (0.003–0.261 mg/kg), hydroxy-2-butanesulfonic acid (0.035–0.445 mg/kg), and butanediols (0.003–0.087 mg/kg). S-2-butyl phosphorothioic acid was a minor metabolite in all intervals (0.004–0.166

mg/kg), while S,S-di-(2-butyl) phosphorodithioic acid was present in 30 and 60 day intervals only, as a minor metabolite (0.004–0.006 mg/kg). Further analysis of the organosoluble metabolites showed the presence of methyl-2-butyl sulfone, and methyl-2-hydroxybutyl sulfone as minor components.

Radiocarbon in the grain was analysed and was found to be primarily due to incorporation into glucose, indicating that the parent chemical undergoes a rapid and facile degradation in the plant.

Nature of the Residue in Radish

The uptake and metabolism of cadusafos in radish was investigated following applications of formulated [^{14}C]cadusafos to soil (17, T. Suzuki, 1999). The ^{14}C-cadusafos was applied to soil at a rate of 9 kg ai./ha, and the radish seeds were sown in the soil. At 50 days after treatment of ^{14}C-Cadusafos, six mature radishes in the three pots were harvested. The radishes were separated into the roots and the foliage for separate analysis. The soil remaining in the pot was also analysed in order to determine the radiochemical balance.

The recoveries of radioactivity in the root, foliage and soil accounted for 0.3%, 1.0% and 70.9% of the applied radioactivity, respectively. The total recovered radioactivity was 72.3% which was the sum of the radioactivity in the root, foliage, soil and water leakage from the pots. The total radioactive residues (TRRs) in the root, foliage and soil were 1.6 mg/kg, 5.0 mg/kg and 10.7 mg/kg equivalents of cadusafos, respectively.

Numerous compounds were detected in the extractable fractions from the root. There were no metabolites which were more than 4%TRR (0.070 mg/kg equivalent of cadusafos). The parent compound was detected at 0.8%TRR (0.014 mg/kg) in the root.

Numerous compounds were detected in the extractable fractions from the foliage. All the metabolites were less than 10%TRR or 0.5 mg/kg except for FMC78121 (19%TRR, 0.88 mg/kg). The parent compound was detected at 0.4% (0.018 mg/kg) in foliage. Many metabolites in the root and foliage were polar compounds which were found in the water-soluble fraction. In the soil no metabolite was greater than 2%TRR.

Since the concentration of radioactivity in the foliage was higher than in the root, it was surmised that cadusafos and its metabolites in the soil were absorbed and translocated to the foliage through the root. Cadusafos and its metabolites were further metabolized to more polar compounds in the radish root and foliage.

Nature of the Residue in Tomato

The uptake and metabolism of cadusafos in tomatoes was investigated following two drip applications of formulated [^{14}C]cadusafos to soil (15, J. Rosenwald, 2008). TRR levels were quantified in the appropriate plant parts (tomato whole fruits, pomace and juice and shoots) and the extractability and nature of the residues were determined.

[^{14}C]cadusafos, formulated as a capsule suspension, was applied by drip irrigation to the soil surface on two separate occasions at a total nominal rate of 6 kg ai/ha. The first application was performed just before transplanting at a rate of 4 kg ai/ha and the second one at 2 kg ai/ha 60 days after the first application. The tomato plants were grown in pots of soil under greenhouse conditions for the entire duration of the study.

Tomatoes were harvested at several intervals: immature tomatoes at pre-maturity intervals (PMI) 21 days (3 days after last application [DALA]), 14 days(10 DALA), 7 days (17 DALA), 2 days (22 DALA), and at maturity (PMI 0, 24 DALA). Additionally soil samples and whole plants (shoot) were taken.

Tomatoes were fractionated into pomace and juice and analysed for their radioactive residues. Juice of PMI 14 and PMI 0 was partitioned with methylene chloride. The aqueous phase was further extracted by C18 solid phase cartridges and eluted sequentially with methanol and water.

The resulting polar aqueous fraction was subjected to acidic hydrolysis using hydrochloric acid. The different fractions were analysed for cadusafos and metabolites by TLC (and HPLC). Additionally, whole plants (shoot) were sampled and analysed for TRR. Surface radioactivity was determined for the tomatoes as well as for the shoots in surface wash samples.

Radioactive residues were mainly taken up via the roots into the shoots, whereas the uptake of residues into fruits was very low. TRR values ranging from 438 to 987 mg parent equivalents (p.e.)/kg were detected in the residual shoots harvested at maturity. The TRR in edible commodities, tomatoes, ranged between 0.028 to 0.093 mg parent equivalents (p.e)/kg in the tomatoes harvested at intervals between PMI 21 to 2. At maturity, the remaining tomatoes showed relatively higher residues (0.126 mg p.e./kg), probably due to the smaller tomato size than prime harvest tomatoes when compared to the other intervals. No radioactive residues were detected in the surface wash samples.

It was observed that the major part of the radioactivity (up to 95%) found in the fruits was present in the tomato juice. Analyses of the tomato juice samples taken at intervals PHI 14 as well as at maturity showed up to 22 radioactive fractions in addition to the parent compound. The parent compound represented up to 6.3% TRR, and butane-2-sulfonic acid up to 6.6% TRR. All other fractions were below 10% TRR, except fraction M11 in the green tomatoes (11.7% TRR). Fraction M11 consisted of several compounds characterised as conjugates. However, none of the radioactive fractions exceeded 0.010 mg p.e./kg tomatoes.

In tomato plants, cadusafos is metabolised via butane-2-thiol to butane-2-sulfonic acid and numerous minor metabolites and conjugates.

Rat and Plant Metabolism Summary

The major metabolic route of cadusafos in rat was through hydrolytic-methylation giving methyl-*sec*-isobutyl sulfide that was further oxidized to hydroxy-sec-isobutylmethylsulfone. In comparison, metabolism of cadusafos in crops such as banana and corn resulted in the formation of hydroxy-sec-isobutylmethylsulfone that was further oxidized to give dihydroxy-sec-isobutylmethylsulfone. In potato the dihydroxy-sec-isobutylmethylsulfone was further oxidized to give the corresponding 1-carboxy-hydroxyisopropylmethylsulfone.

Environmental fate in soil

The Meeting received information on aerobic degradation of cadusafos in soil and field dissipation studies performed in the USA and in Europe (Germany and Spain).

Aerobic soil degradation [USA Studies]

Silt loam and sandy loam soil samples were treated with radiolabelled cadusafos at approximately 3.0 mg/kg and analysed at the following intervals: 0, 7, 14, 30, 60, and 120 days (20, J.L. Reynolds, 1984) and at 0, 7, 14, 30, 45, 60, and 90 days (22, S.S. Singer, 1993). All soil samples were maintained at 25 ± 1ºC in the absence of light during the study. The soil properties are summarised in Table 4.

Table 4 Soil properties in USA aerobic soil degradation studies

Soil	Texture - %			Organic Carbon (%)	CEC [a]	pH	Location
	Sand	Silt	Clay				
Hagerstown silt loam	20.8	54.8	24.0	1.3	13.8	7.5	Beltsville, MD
Cosad sandy loam	54.4	35.2	10.4	1.7	16.1	7.0	Wilson, NY
Georgetown silt loam	22.4	52.4	25.2	4.5	13.2	7.4	Georgetown, KY

[a] Cation exchange capacity expressed as meq/100 g.

Analysis of cadusafos in Hagerstown silt loam soil showed that 22.8% of the applied compound remained 120 DAT. Bound residues and evolved $^{14}CO_2$ comprised 32 and 43%,

respectively. Several degradates were detected at the final sampling interval, but no single compound exceeded 1.7% of the applied dose, see Table 5.

Table 5 Hagerstown silt loam: normalized [a] percent distribution of total recovered ^{14}C

% of radioactivity	Interval (days)					
	0	7	14	30	60	120
FMC 67825	94.2	85.1	76.6	61.4	39.3	22.8
Unidentified Products	4.0	3.3	3.6	3.5	1.8	1.4
Total % extractable	98.2	88.4	80.2	64.9	41.1	24.2
Aqueous	0.8	1.7	2.7	2.2	1.6	1.0
$^{14}CO2$	-	0.6	1.9	8.7	26.5	42.9
Residues bound	1.0	9.3	15.2	24.2	30.8	31.9
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0

Similar results were reported for the Cosad sandy loam soil samples. Parent declined to 14.5% of the total residue while unextracted residues and evolved $^{14}CO_2$ amounted to 32 and 51%, respectively. No single degradate exceeded 1.5% of the total ^{14}C residue at any time interval.

Table 6 Cosad sandy loam : normalized [a] percent distribution of total recovered ^{14}C

% of radioactivity	Interval (days)					
	0	7	14	30	60	120
FMC 67825	94.7	85.9	77.0	58.0	42.5	14.5
Unidentified Products	4.0	4.1	4.0	2.7	1.5	0.7
Total % extractable	98.7	90.0	81.0	60.7	44.0	15.2
Aqueous	0.3	2.0	3.3	1.6	1.4	1.8
$^{14}CO2$	-	0.8	3.8	14.8	28.2	51.2
Residues bound	1.0	7.2	11.9	22.9	26.4	31.8
TOTAL	100.0	100.0	100.0	100.0	100.0	100.0

Because over 30% of the total radioactivity was characterised as bound residues in the 120 DAT samples, additional analyses of the post extraction solids was conducted following approximately one year of aging (21, S.S. Singer, 1988). Most of the radioactivity was successfully released from these samples following acid (0.25 N HCl) and base (0.1 N NaOH) digestion procedures, which allowed further clarification of the residue distribution as presented in Table 7.

Table 7 Distribution of radiolabelled residues and FMC 67825 removed from 2 soils at 120 days

Soil	Hagerstown silt loam		Cosad sandy loam	
Fractions	% ^{14}C	% FMC 67825	% ^{14}C	% FMC 67825
MeCl2/CH3CN	26.8	25.2	16.8	14.5
EtOAc (IV)	3.5	3.3	2.5	2.3
Acetone (V)	3.1	2.8	0.9	0.8
EtOAc (VIII)	0.6		0.8	
Aqueous (VI)	8.1		6.2	
Fulvic acid (XI)	10.3		11.7	
Humic acid (XII)	3.6		5.9	
Residual solids (X)	2.2		2.4	
CO2	40.9		50.8	
Total	100.0	31.3	99.9	17.6

Acid and base refluxing procedures were effective at removing significant levels of radioactivity from the post-extraction solids. Parent cadusafos constituted the major portion of the residue released by acid digestion. The residues extracted by base digestion were found to be associated with fulvic and humic acid compounds.

For the Georgetown silt loam soil, nearly complete degradation of parent cadusafos was observed by 90 DAT, where only 1.5% of the applied material was found. One degradate, identified as methyl sec-butyl sulfone, was found at a maximum level of 7.5% of the applied radioactivity at 14 DAT, see Table 8.

Table 8 % TRR and mg/kg for identified degradates in silt loam soil.

Time	Cadusafos		Methyl sec-butyl sulfone	
	%	mg/kg [a]	%	mg/kg [b]
0	102.0	3.10	0.00	0
7	67.9	2.06	5.40	0.164
14	47.3	1.44	7.46	0.227
30	18.8	0.57	2.75	0.084
45	8.0	0.24	0.65	0.020
60	2.9	0.09	0.18	0.005
90	1.5	0.05	0.06	0.002

[a] mg/kg = % TRR x 3.04 mg/kg treatment

[b] mg/kg equivalent to parent

Degradation times were determined for all three soils studied and are summarised in Table 9. No explanation was provided for the significantly shorter degradation time found in the Georgetown silt loam as compared to the Hagerstown and Cosad soils.

Table 9 Degradation time of FMC 67825

Soil Studied	DT_{50} (days)
Hagerstown silt loam	45
Cosad sandy loam	45
Georgetown silt loam	11.3

Conclusions: Cadusafos is intensely mineralized; the estimated time to 50% degradation (DT50) was 45 days in soils tested in the 1984 study. Several degradates were detected, however, none exceeded 1.7% of the total radioactive residue at any time interval. In comparison, the 1993 study reported DT50 times of 11.3 days for cadusafos and 10.6 days for methyl sec-butyl sulfone in the Georgetown silt loam soil.

Aerobic soil degradation [European (Germany and Spain) Studies]

Loam and clay loam soil samples were treated with radiolabelled cadusafos at a rate corresponding to the maximum field application rate of 5 kg ai/ha (3.3 mg/kg), and analysed at the following intervals: 0, 7, 14, 28, 42, 64, and 100 days (18, J. Baumann and J. Ferreira, 2001a). All soil samples were maintained at 20 ± 2 ºC in the absence of light during the study. The soil properties are summarised in Table 10.

Table 10 Soil properties in European aerobic soil degradation studies.

Location	Hofheim, Germany	Enkheim, Germany	Alcada del Rio, Spain
% sand	24.4	2.7	27.9
% silt	51.5	67.1	50.5
% clay	24.1	30.1	21.6

Location	Hofheim, Germany	Enkheim, Germany	Alcada del Rio, Spain
Texture	loam	clay loam	loam
% Organic Matter	1.79	3.8	2.7
CEC*	98.1	122	72.9
pH	5.8	6.8	7.3
WHC* (%)	35.9	37.3	67.7
Biomass (µg/g soil) n = 3	83.0 ± 15.6	96.7 ± 1.0	66.7 ± 2.8

* CEC : Cation exchange capacity in mval/kg dw

WHC : Water holding capacity

Analysis of cadusafos in these three soils demonstrated comparable degradation times as summarised in Table 11.

Table 11 Residues of applied dose of cadusafos in test soils

	Hofheim, Germany		Enkheim, Germany		Alcala del rio, Spain	
Day (d)	Average (mg/kg)	Percent app. dose (%)	Average (mg/kg)	Percent app. dose (%)	Average (mg/kg)	Percent app. dose (%)
0	2.309	100	2.186	100.0	2.262	100.0
7	1.707	73.9	1.726	78.9	2.161	95.5
14	1.736	75.2	1.598	73.1	2.315	102.3
28	1.620	70.2	1.484	67.9	1.639	72.5
42	1.552	67.2	1.315	60.2	1.375	60.8
64	1.106	47.9	1.090	49.9	0.980	43.3
100	0.520	22.5	0.583	26.7	0.542	24.0

Based on the above results, the following DT50 and DT90 times shown in Table 12 were calculated.

Table 12 Degradation time of cadusafos in three soils

	Hofheim	Enkheim	Spain
DT_{50} (days)	62.4	61.9	51
DT_{90} (days)	207	206	169.3

Degradation of Cadusafos Applied as Formulated Product

In order to investigate the rate of aerobic soil degradation of cadusafos applied in the field as formulated, a separate study was conducted using applications of 200 CS (19.5% active ingredient) and 10 GR (containing 10% active ingredient) formulations to soil samples in Hofheim, Germany (19, J. Baumann and J. Ferreira, 2001b). The maximum field application rate of 5 kg ai/ha (3.3 mg/kg) was used and samples were analysed at the following intervals: 0, 7, 14, 28, 42, 64, and 100 days. All soil samples were maintained at 20 ± 2ºC in the absence of light during the study.

From this study, the DT_{50} and DT_{90} values of cadusafos were determined as summarised in Table 13. The formulation apparently has minimal effect on the rate of soil degradation of cadusafos.

Table 13 Degradation time of cadusafos following application of CS and GR formulations

	200 CS	10 GR
DT_{50} (days)	45	48.8
DT_{90} (days)	149.5	162.2

Rotational Crops

No rotational crop studies were submitted for review. For rotated crops after potatoes there would be no expectation of residues remaining in the soil following an early season application to potato. Cadusafos degrades rapidly in soil, having a relatively short estimated half-life in soil of about 45 days.

Photolysis

The Meeting received photolysis studies of cadusafos in soil.

Photodegradation in Soil

Sandy loam soil samples were exposed to natural sunlight (11 hour photo periods per day) following treatment with radiolabelled cadusafos at approximately 1 mg/kg and analysed at the following intervals: 0, 3, 7, 14, 21, and 30 days (06, R.H. Tullman, 1988a). Identical samples were wrapped in foil to serve as dark controls. The temperature of the 5 gram soil samples were maintained at 23.6°C ± 4.1 over the course of the study. Analysis was performed by LSC/combustion to determine the radioactivity recovery. The results are summarised in Table 14.

Table 14 Material extraction of soil samples, per cent of applied radioactivity

% of applied		0	3	7	14	21	30
Irradiated	FMC 67825	100.0	99.2	99.5	99.3	99.2	98.9
	Acids		0.8	0.4	0.8	0.8	1.0
Dark control	FMC 67825	100.0	99.7	100.0	100.0	100.0	100.0
	Acids		0.2				

The residues designated as "Acids" comprised three compounds whose sum was ≤ 1.0% of the total radioactivity at all time intervals examined.

The result of this study shows that cadusafos is photochemically stable in/on soil surfaces. The slow photochemical degradation is in line with the low UV/visible absorbance of cadusafos.

Hydrolysis in Water

Buffered aqueous solutions (pH 5, 7. and 9) containing approximately 3 mg/L of radiolabelled cadusafos were analysed for hydrolysis at the following intervals: 0, 3, 6, 10, 13, 17, 20, 24, 27, and 34 days after treatment (24, S. Witkonton, 1986). All samples were maintained at 25°C in the absence of light. The solutions were analysed by HPLC and product identification was by GC/MS. The results are summarised in Table 15.

Table 15 Distribution of radioactivity according to the pH

pH = 5	% ^{14}C Distribution at Various Time Intervals (Days)									
Product	0	3	6	10	13	17	20	24	27	34
FM 67825	102.6	105.8	112.7	106.0	103.2	99.6	101.3	100.5	103.6	102.8
OSPA	0.2	0.3	0.6	0.6	1.1	1.3	1.4	1.7	1.9	2.4
di-sec-butyl disulfide	0.4	0.2	0.5	0.4	0.3	0.4	0.4	0.2	0.2	0.2
Sec-butyl mercaptan	0.5	0.1	0.2	0	0	0	0	0	0.1	0.2
Total Percent Recovered	103.9	106.7	114.4	107.6	104.9	101.5	103.5	102.8	106.0	105.7

pH = 7	% ^{14}C Distribution at Various Time Intervals (Days)									
Product	0	3	6	10	13	17	20	24	27	34

pH = 7	% ^{14}C Distribution at Various Time Intervals (Days)									
Product	0	3	6	10	13	17	20	24	27	34
FM 67825	99.3	111.3	106.3	106.0	103.2	105.1	104.0	103.6	105.0	103.6
OSPA	0.1	0.3	0.3	0.4	0.6	0.4	1.4	1.2	1.8	2.3
di-sec-butyl disulfide	0.1	0.3	0.3	0.4	0.3	0.4	0.1	0.2	0.2	0.1
Sec-butyl mercaptan	0	0.2	0.1	0	0	0	0.1	0	0.1	0.1
Total Percent Recovered	99.7	112.3	107.5	107.3	104.9	107.0	105.7	105.7	107.3	106.3

pH = 9	% ^{14}C Distribution at Various Time Intervals (Days)									
Product	0	3	6	10	13	17	20	24	27	34
FM 67825	106.2	107.8	102.6	105.4	102.7	102.8	97.7	107.2	95.9	90.6
OSPA	0.1	0.8	1.9	3.0	4.3	5.5	6.3	8.3	8.4	10.0
di-sec-butyl disulfide	0.1	0.3	0.4	0.5	0.8	0.9	0.5	1.2	0.7	0.8
Sec-butyl mercaptan	0.5	0.2	0	0	0	0	0	0.1	0	0.1
Total Percent Recovered	107.0	109.8	105.6	109.4	107.9	109.4	104.8	117.0	105.4	101.8

Cadusafos was stable at pH 5 and 7 during the 34 day study period. At pH 9, slow hydrolysis was observed that formed O-ethyl-S-(2-butyl) phosphorothioic acid (OSPA), which comprised up to 10% of the radioactivity by day 34. At pH 9, the half-life is calculated to 178.9 days by extrapolation, while cadusafos was stable at lower pHs.

Residue Analytical Methods

The Meeting received information on residue analytical methods for cadusafos in plant samples. Independent laboratory validation results were also provided.

Banana Analysis

Cadusafos residues in/on banana matrices were extracted by blending with ethyl acetate (25, I.A. Macdonald, 1985). Anhydrous sodium sulphate was added to the mixture and it was re-macerated and filtered through glass wool. The extract was concentrated and taken up with hexane. Further clean up was achieved using a chromatographic column packed with an alumina slurry. Quantitative determination of the active substance was performed using gas chromatography equipped with a flame photometric detector.

The limit of quantitation for banana matrices was 0.005 mg/kg. The limit of detection was 0.002 mg/kg, and method recoveries ranged from 79–109%.

Banana, Potato, and Corn Grain, Silage, and Stover Analysis

Residues of cadusafos in bananas, potatoes and corn matrices were extracted by blending the processed sample with a methanol/water mixture, gravity filtering though glass wool and partitioning with methylene chloride (28, T.C. Schreier, 1987). The organic phase was filtered through anhydrous sodium sulfate, concentrated and taken up with hexane. Further clean up was achieved using silicagel SEP PAK cartridges and eluting cadusafos with 25% ethyl acetate in hexane. Quantitative determination of the active substance was performed using gas chromatography and an NP-FID detector (GC-NPD).

The limit of quantitation was 0.1 mg/kg for bananas, 0.2 mg/kg for potatoes, and 0.05 mg/kg for corn. The limit of detection was 0.02 mg/kg for bananas, 0.04 mg/kg for potatoes, and 0.01 mg/kg for corn. Method recoveries ranged from 59–81% for bananas, 68–76% for potatoes, and 60–96% for corn matrices.

Improved Method for Banana, Potato, Strawberry, Bean, Pepper, and Melon Analysis

The methods described above were improved for bananas, potatoes and other crops (26, M.M. McChesney, 1998). Minor changes included backwashing the dichloromethane phase with water to remove methanol and changing the composition of the eluent from silicagel cartridges to 15% ethylacetate in hexane. The sensitivity of the method was improved by using a flame photometric detector operating in phosphorous mode.

The limit of quantitation was 0.001 mg/kg for banana pulp and 0.005 mg/kg for the other crops. The limit of detection was 0.0002 mg/kg for banana pulp and 0.001 mg/kg for the other crops. Method recoveries ranged from 80–94% for banana pulp and 87–94% for potatoes. Table 16 summarises the recovery results obtained.

Table 16 Recovery Results in Fortified Crop Matrices

Matrix	Fortification Level (mg/kg)	Mean Recovery [a]	Standard Deviation
Banana Pulp	0.001	86	4.7
	0.005	84	10
	0.010	80	4.1
	0.20	94	5.8
Banana Pulp + Peel	0.001	94	6.2
	0.005	85	8.4
	0.010	80	7.3
	0.20	94	3.6
Green Beans	0.005	83	9.2
	0.010	89	3.4
	0.020	97	3.8
	0.20	88	4.0
Melons	0.005	97	8.3
	0.010	89	1.4
	0.020	95	5.3
	0.20	96	2.7
Pepper	0.005	94	5.5
	0.010	99	5.3
	0.020	97	4.1
	0.20	87	4.8
Potato	0.005	89	12
	0.010	88	4.9
	0.020	94	4.5
	0.20	87	7.7
Strawberry	0.005	92	9.4
	0.010	90	7.8
	0.020	93	2.6
	0.20	83	5.4

[a] Five replicates at each fortification level.

Independent Laboratory Validations

Successfully independent laboratory validation of the analytical method for analysis of cadusafos in a variety of plant matrices described in reference 28, T.C. Schreier, 1987, was reported, with a limit of quantitation of 0.01 mg/kg (29, M. Verdelet, 1994). The independent laboratory was Battelle–Geneva Research Centres, Agrochemical Product Development. Separate samples of tomato, cucumber, eggplant, and soil were fortified in duplicate with cadusafos at 0.01, 0.10, and 0.50 mg/kg. Most recoveries were within 70 and 110%, with only two samples (121 and 115%, in one tomato and one eggplant sample, respectively) being outside the standard range.

Successfully independent laboratory validation of the analytical method for analysis of cadusafos in a variety of plant matrices described in reference 28, T.C. Schreier, 1987, was reported, with a limit of quantitation of 0.01 mg/kg in potato (30, M. Weidenauer, 1999). The independent laboratory was Battelle–Geneva Research Centres, Agrochemical Product Development. Separate

samples of potato were fortified in quintuplicate with cadusafos at 0.002 and 0.02 mg/kg. All recoveries were within 70 and 110%, and standard deviations were 6.8 and 11.8 for the 0.002 and 0.02 mg/kg fortification levels, respectively.

Successfully independent laboratory validation of the analytical method for analysis of cadusafos in a variety of plant matrices described in reference 26, M.M. McChesney, 1998, was reported, with a limit of quantitation of 0.005 mg/kg for banana and tomato (27, O. Pigeon, 2005). The independent laboratory was the Pesticide Research Department at Walloon Agricultural Research Centre in Gemblox, Belgium. The analytical procedure consisted of a water/methanol extraction, a dichloromethane partition and a silica gel clean-up procedure. The final cadusafos analysis was done by GC/NPD. Qualitative and quantitative confirmations were performed by Capillary Gas Chromatography with Mass Spectrometry Detection (GC-MS). Separate samples of banana and tomato were fortified in quintuplicate with cadusafos at 0.005 and 0.05 mg/kg. For banana samples fortified at the LOQ of 0.005 mg/kg, the average recovery was 106% (n = 5, RSD = 5.9%), and at 0.05 mg/kg, the average recovery was 96% (n = 5, RSD = 5.1%). For tomato samples fortified at the LOQ of 0.005 mg/kg, the average recovery was 99% (n = 5, RSD = 6.1%), and at 0.05 mg/kg, the average recovery was 93% (n = 5, RSD = 7.0%).

Adequate analytical methods are available for determination of cadusafos residue levels in banana and potato samples. Modifications have been made to improve the method sensitivity over the years. Successful independent laboratory validations of these methods have been conducted.

No information regarding the recovery of cadusafos through multiresidue methods was submitted. However, organophosphate compounds are generally amenable to analysis by multiresidue methods and the Pesticide Data Program of the United States Department of Agriculture has reported monitoring results for cadusafos residues in banana samples.

Stability of pesticide residues in stored analytical samples

The Meeting received information on the stability of cadusafos in freezer-stored samples of banana, potato, and corn (54, Schreier, 1987b). The samples were fortified at 0.10 or 0.20 mg/kg and stored at -20 °C for up to 15 months. Three replicates were analysed at each sampling interval using the method reported by Schreier (28, Schreier, 1987a). The concurrent recoveries were in the range of 98–100%, with RSDs of 4.0–6.4%. The results are summarised in Table 17, showing that cadusafos was stable under freezer-storage conditions during the tested storage interval of 14–15 months.

Table 17 Storage Stability Study Results for Residues of Cadusafos in Plant Matrices

Matrix	Fortification level (mg/kg)	6-month analysis	Percent remaining	14-15 month analysis	Percent remaining
Banana	0.10	0.12	120	0.10	100
	0.10	0.08	80	0.09	90
	0.10	0.09	90	0.10	100
Potato	0.20	0.22	110	0.20	100
	0.20	0.21	105	0.27	135
	0.20	0.20	100	0.22	110
Corn, grain	0.10	0.09	90	0.09	90
	0.10	0.10	100	0.09	90
	0.10	0.09	90	0.09	90
Corn, silage	0.20	0.24	120	0.21	105
	0.20	0.18	90	0.21	105
	0.20	0.16	80	0.21	105
Corn, stover	0.20	0.23	115	0.22	110
	0.20	0.23	115	0.24	120
	0.20	0.23	115	0.26	130

USE PATTERN

Cadusafos is applied primarily as a granular formulation and has registered uses in or on banana and potato. The GAPs are summarised by commodity and country in Table 18.

Table 18 Cadusafos Use Patterns for Banana and Potato

Crop	Country	Formulation	Method	Rate (g ai/plant)	Number of Applications	PHI
Bananas	Belize	G 100 g/kg	Ground	2	3	ns [a]
Bananas	Costa Rica	G 100 g/kg	Ground	2	3	ns
			Ground	3	2	ns
Bananas	Dominican Republic	G 100 g/kg	Ground	2	3	ns
			Ground	3	2	ns
Bananas	Ecuador	G 100 g/kg	Ground	2	2	ns
Bananas	Guatemala	G 100 g/kg	Ground	2	3	ns
				3	2	ns
Bananas	Honduras	G 100 g/kg	Ground	2	3	ns
Bananas	Ivory Coast	G 100 g/kg	Ground	2	2–3	ns
Bananas	Mexico	G 100 g/kg	Ground	2–3	2	60
Bananas	Philippines	G 100 g/kg	Ground	2.5–3	2	ns
				2	3–4	ns
Crop	Country	Formulation	Method	Conc (kg ai/ ha)	Number Applications	PHI
Potatoes	Brazil	G 100 g/kg	Ground	3	1	90
Potatoes	Mexico	G 100 g/kg	Ground	4–5	1	144

[a] ns = not specified

RESIDUES RESULTING FROM SUPERVISED TRIALS

The Meeting received supervised trial data for cadusafos uses on bananas and potatoes. In most trials, cadusafos was applied as a granular formulation.

Bananas

A total of eighteen banana trials were reported from numerous countries. These trials were conducted at a variety of application rates and a wide range of PHIs. No detectable residue levels were found in banana pulp samples and only low levels were reported in peels. Table 19 summarises the results.

Table 19 Residues in bananas from residue trials conducted with cadusafos in Australia, Costa Rica, Ecuador, Guatemala, Honduras, Ivory Coast, France, Mexico, and Philippines

Banana Country (Year) Location (Variety)	Application rate		Portion analysed	Residues (mg/kg)	PHI (days)	Reference & Comments
	g ai/plant	no				
Australia, 1987 Yandina (Cavendish)	3.0	3	Peel Pulp	< 0.005 < 0.005	13 13	Ref : 44
Costa Rica, 1985 Guapiles (Cavendish)	2 2 10 10 20 20	2	Peel Pulp Peel Pulp Peel Pulp	< 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005	27 27 27 27 27 27	Ref : 40

Banana Country (Year) Location (Variety)	Application rate g ai/plant	 no	Portion analysed	Residues (mg/kg)	PHI (days)	Reference & Comments
Costa Rica, 1986 Finca San Lucas (Cavendish)	3	1	Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp	< 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005	10 10 30 30 60 60 90 90 120 120 160 160	Ref: 32 3 plots identical results
Costa Rica, 1986 Valley Estrella (Cavendish)	3.6	4	Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp	< 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005	1 1 5 5 15 15 30 30 60 60 90 90	Ref: 33
Costa Rica, 1986 Finca Cobal	10 20	1	Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp	0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005	10 10 30 30 60 60 90 90 10 10 30 30 60 60 90 90	Ref: 38
Costa Rica, 1987 Waldec (Giant Cavendish)	3.0	1	Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp	< 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005	10 10 30 30 120 120 160 160 10 10 30 30	Ref: 42
Costa Rica, 1987 Finca La Guajira, Limon (Giant Cavendish)	3.0	1	Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp	< 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005	120 120 160 160 10 10 30 30 120 120 160 160	Ref: 42

Banana Country (Year) Location (Variety)	Application rate		Portion analysed	Residues (mg/kg)	PHI (days)	Reference & Comments
	g ai/plant	no				
Ecuador, 1986 El Triunfo/Guayas (Cavendish)	3	1	Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp	< 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005	30 30 60 60 90 90 120 120 160 160	Ref: 36
Guatemala, 1985	10.8	1	Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp	< 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005	10 10 30 30 60 60 90 90 120 120 160 160	Ref: 34
Honduras, 1986	10.8	1	Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp	< 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005	10 10 30 30 60 60 90 90 120 120 160 160	Ref: 39
Honduras, 1987 Higuerito (Grand Nain)	5	1	Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp	< 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005	30 30 60 60 90 90 120 120 160 160	Ref: 42
Ivory Coast, 1984 Aboisso (Poyo)	2 4	3	Peel Pulp Peel Pulp	< 0.005 < 0.005 < 0.005 < 0.005	43 43 43 43	Ref: 41

Banana Country (Year) Location (Variety)	Application rate		Portion analysed	Residues (mg/kg)	PHI (days)	Reference & Comments
	g ai/plant	no				
Ivory Coast, 1986 Adidjan (Poyo)	4	1	Peel	< 0.005	3	Ref: 31
			Pulp	< 0.005	3	
			Peel	< 0.005	7	
			Pulp	< 0.005	7	
			Peel	< 0.005	14	
			Pulp	< 0.005	14	
			Peel	< 0.005	30	
			Pulp	< 0.005	30	
			Peel	< 0.005	62	
			Pulp	< 0.005	62	
			Peel	< 0.005	92	
			Pulp	< 0.005	92	
	6		Peel	< 0.005	3	
			Pulp	< 0.005	3	
			Peel	< 0.005	7	
			Pulp	< 0.005	7	
			Peel	< 0.005	14	
			Pulp	< 0.005	14	
			Peel	< 0.005	30	
			Pulp	< 0.005	30	
			Peel	< 0.005	62	
			Pulp	< 0.005	62	
			Peel	< 0.005	92	
			Pulp	< 0.005	92	
Martinique, 1986 Fort de France (Grande naine)	6	1	Peel	0.022	0	Ref: 37
			Pulp	< 0.005	0	
			Peel	< 0.005	3	
			Pulp	< 0.005	3	
			Peel	< 0.005	7	
			Pulp	< 0.005	7	
			Peel	0.009	15	
			Pulp	< 0.005	15	
			Peel	< 0.005	30	
			Pulp	< 0.005	30	
			Peel	< 0.005	60	
			Pulp	< 0.005	60	
			Peel	< 0.005	90	
			Pulp	< 0.005	90	
	9		Peel	< 0.005	0	
			Pulp	< 0.005	0	
			Peel	0.008	3	
			Pulp	< 0.005	3	
			Peel	0.008	7	
			Pulp	< 0.005	7	
			Peel	0.010	15	
			Pulp	< 0.005	15	
			Peel	0.007	30	
			Pulp	< 0.005	30	
			Peel	< 0.005	60	
			Pulp	< 0.005	60	
			Peel	< 0.005	90	
			Pulp	< 0.005	90	

Banana Country (Year) Location (Variety)	Application rate		Portion	Residues	PHI	Reference & Comments
	g ai/plant	no	analysed	(mg/kg)	(days)	
Mexico, 1986 Tapachula, Chiapas (Gran nain)	6.6	2	Peel Pulp Peel Pulp Peel Pulp Peel Pulp Peel Pulp	< 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005	10 10 30 30 60 60 120 120 150 150	Ref: 35
Philippines, 1988 Davao (Cavendish)	2	4	Peel Pulp Peel Pulp Peel Pulp Peel Pulp	< 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005 < 0.005	13 13 27 27 55 55 83 83	Ref: 43
Philippines	2	1	Peel Pulp Whole Peel Pulp Whole Peel Pulp Whole Peel Pulp Whole Peel Pulp Whole Peel Pulp Whole	< 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02	21 21 21 35 35 35 49 49 49 63 63 63 77 77 77 91 91 91	Ref: 45
	3		Peel Pulp Whole Peel Pulp Whole Peel Pulp Whole Peel Pulp Whole Peel Pulp Whole Peel Pulp Whole	< 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02 < 0.02	21 21 21 35 35 35 49 49 49 63 63 63 77 77 77 91 91 91	

Potato

A total of nine potato field trials were reported to the Meeting. All trials made use of granular formulations of cadusafos. These trials span a range of application rates and PHI, but all demonstrate

residue levels near the method LOQ. Trials from Spain and Greece were provided although registrations for use of cadusafos on potatoes is no longer supported. The results of the submitted studies are summarised in Table 20.

Table 20 Residues in potato (tubers) from residue trials conducted with cadusafos granular formulations in Brazil, Greece, Mexico, and Spain

POTATO Country (Year) Location (Variety)	Application rate				Residues (mg/kg)	PHI (days)	Reference & Comments
	kg ai/ha	water L/ha	kg ai/hL	no	Tubers		
Brazil, 1998 Fazenda Sao Carlos (Bintge)	3 6			1	< 0.02 < 0.02	60	Ref: 46
Greece, 1989 Drama (Spounta)	4 5 6			1	< 0.005 < 0.005 0.005	148	Ref: 52
Greece, 2001 Polymylos, Kozani (Spounta)	5			1	< 0.01	119	Ref: 47
Mexico, 1997 Hidalgo (Rosita)	5			1	0.008	144	Ref: 53
Mexico, 1997 Nuevo Leon (Alpha)	5			1	< 0.005 (0.004)[a]	119	Ref: 53
Mexico, 1998 Tlalcontena, Veracruz (Yema)	3 6			1	< 0.01 < 0.01	193	Ref: 51
Spain, 2001 Villanueva (Fabula)	5			1	0.03	88	Ref: 48 :
Spain, 1988 Sa Pobla Mallorca (Mary Bar)	10 14 28			1	0.008 0.012 0.026	85 85 85	Ref: 49
Spain, 1988 Sa Pobla Mallorca (Mary Bar)	10 14 28			1	0.004 0.007 0.025	114 114 114	Ref: 50

[a] Value in parentheses was reported being between the LOQ of 0.005 mg/kg and the LOD of 0.001 mg/kg.

FATE OF RESIDUES IN PROCESSING

The Meeting received four processing studies for potato.

In the first study, a capsule suspension formulation (CS) was applied in a field trial in Belgium at a rate of 4.5 kg ai/ha (56, N. Ginzburg and M. Weidenauer, 1999a). Potato samples were taken from the treated and control plots at harvest, but no PHI was specified. Samples of uncooked whole potatoes and peels were analysed. Processing involved the preparation of boiled potatoes and French fries, using typical commercial procedures. No residues were detected in the processed potato commodities; low levels were found in the unprocessed whole potatoes and peels, see Table 21.

In the second study, a CS formulation was applied in a field trial in Belgium at a rate of 4.5 kg ai/ha (57, N. Ginzburg and M. Weidenauer, 1999b). Potato samples were taken from the treated and control plots at harvest, but no PHI was specified. Samples of uncooked whole potatoes were analysed. Processing involved the preparation of boiled potatoes (with peels) and jacket potatoes, using typical commercial procedures. These samples and boiled potato peels were analysed for cadusafos residues. No residue concentration was observed in the processed potato commodities, see Table 21.

In the third and fourth studies, CS formulations were applied in field trials in Belgium and the Netherlands at a rate of approximately 25 kg ai/ha (55, M.A. Enriquez, 2001). The potato processing and analysis of the resulting processed potatoes was as in the second study, however, the PHIs were reported as 106 and 136 days, in the Belgium and Netherland studies, respectively. Again, no residue concentration was observed in the processed potato commodities, see Table 21.

Samples from four potato residue studies performed with CS formulations were processed into boiled potatoes, jacket potatoes, and fried potatoes. Residue levels are shown in Table 21. Processing results in reduced cadusafos residue levels except for peel, where residues concentrated to give a processing factor of 7.5× for unboiled samples. After boiling, residues in the peel were lower than in the whole potato (unboiled).

Table 21 Residues in processed commodities of potatoes from residue trials conducted with cadusafos in Belgium and Netherlands

Potato Country (Year) Location (Variety)	Application rate			Portion	Residues	PHI	Reference &
	kg ai/ha	water L/ha	no	analysed	(mg/kg)	(days)	Comments
Belgium, 1999	4.5	22.5	1	Whole Peel Peeled potato Boiled potato Fried potato	0.02 0.15 < 0.01 < 0.01 < 0.01	NS	Ref : 56 Peel residue from unboiled potatoes.
Belgium, 1999	4.5	22.5	1	Whole Peel Peeled potato Boiled potato	0.05 0.03 < 0.01 < 0.01	NS	Ref : 57 Peel residue from boiled potatoes.
Saint Amand, Belgium, 2001	25	125	1	Whole Peel Peeled potato Boiled potato	0.03 0.01 < 0.01 < 0.01	106	Ref: 55 Peel residue from boiled potatoes.
Wijnandsrade, The Netherlands, 2001	25	125	1	Whole Peel Peeled potato Boiled potato	0.04 0.02 < 0.01 < 0.01	136	Ref: 55 Peel residue from boiled potatoes.

NS = Not specified

RESIDUES IN ANIMAL COMMODITIES

Farm animal feeding studies

A bovine feeding study was not provided. However, there are no cattle feed items resulting from the RACs for which the 2010 Meeting made maximum residue level recommendations, and hence, no need for a bovine feeding study.

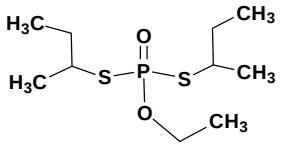
A poultry feeding study was not provided. However, there are no poultry feed items resulting from the RACs for which the 2010 Meeting made maximum residue level recommendations, and hence, no need for a poultry feeding study.

APPRAISAL

Cadusafos is an organophosphate nematicide. It was evaluated by JMPR 1991(T, R), 1992(R). It was evaluated for toxicological review by JMPR in 2009 as the periodic re-evaluation. The ADI for cadusafos was established as 0–0.0005 mg/kg bw and acute reference dose was 0.001 mg/kg bw

Cadusafos was scheduled at the Forty-first Session of the CCPR (2009) for the periodic re-evaluation of residues by the 2010 JMPR.

Residue studies were submitted by the manufacturer to support the use of cadusafos in or on banana and potatoes.



Animal metabolism

The 2009 JMPR Meeting reviewed studies on the metabolism of ^{14}C-labelled cadusafos in rats. These studies showed that more than 80% of the administered dose was excreted within 24 hours, and more than 90% within 48 hours. Of the recovered radiolabel, 70–80% was found in the urine, 4–14% in the faeces, and 12–18% as CO_2. Cadusafos residues were widely distributed among rat organs, with a peak of 1.2% of the administered dose being found in the body at 7 days after dosing. Highest TRR concentrations were found in the liver, fat, kidney, and lungs. There was no evidence for accumulation of cadusafos residues in the body.

Cadusafos is extensively metabolized in rats. Metabolism proceeds by cleavage of one of the thio-butyl groups to give *sec*-butyl mercaptan and O-ethyl-S-(2-butyl) phosphorothioic acid, which can then be cleaved to S-(2-butyl) phosphorothioic acid or O-ethyl phosphorothioic acid. *Sec*-Butyl mercaptan is biotransformed to methyl *sec*-butyl sulfide, sulfoxide, and sulfone; and then to hydroxysulfones. Alternatively, *sec*-butyl mercaptan can be oxidized to butyl sulfonic acid, then ethyl and methyl sulfonic acid. CO_2 formation may proceed from *sec*-butyl mercaptan or from sulfonic acid. Carbon dioxide is incorporated into urea or other endogenous substances. No significant differences in the metabolic profile of cadusafos in male and female rats were reported.

No livestock metabolism studies were available for consideration since there are no relevant livestock feed items. Based on the results of the rat metabolism studies, cadusafos metabolism in animals consists of an initial hydrolysis reaction followed by a series of oxidation and/or methylation reactions to produce a variety of small, polar compounds.

Plant Metabolism

Cadusafos metabolism studies were submitted on the following plants: banana, potato, corn, radish, and tomato. The studies on plant metabolism all involved applications to soil, consistent with intended use patterns. Cadusafos metabolism was relatively consistent in these matrices: hydrolytic cleavage followed by a series of oxidation reactions to give several small, polar compounds. In addition, conjugation with glucose was reported. The primary difference noted between plants was the extent of metabolism observed, with potato demonstrating the most extensive metabolism.

Banana

Two banana plants in the early fruiting stage were treated with [^{14}C]-cadusafos at the rate of 3.0 g ai per tree applied to the soil. Mature fruit and leaves from the plants were harvested and analysed. Initial combustion analysis indicated only low levels of total radioactive residue (TRR) in the fruit, 0.051 mg/kg in ripe pulp and 0.031 mg/kg in unripe pulp. Extraction and partition analysis of radiocarbon residue in ripe banana pulp and peel showed that the majority of the residue consisted of water-soluble polar metabolites with lower levels of organo-soluble metabolites. No parent chemical was detected in the ripe or unripe fruit (i.e., < 1 ppb), whereas 1 ppb of parent chemical was found in the leaf. The predominant residue identified in unripe pulp was methyl 2-butyl sulfone (36% TRR, 0.011 mg/kg). As bananas ripen to yellow, an additional oxidation step occurs resulting in hydroxy 2-butyl methylsulfone being the predominate metabolite observed in ripe pulp (52% TRR, 0.027 mg/kg).

Potato

Radiolabelled cadusafos was applied to soil in pots at a rate equivalent to 6 kg ai/ha. Potatoes were planted into the pots of treated soil and maintained in a greenhouse for 44 days, at which time they were moved to an outdoor screen house until maturity. The potatoes were harvested at normal maturity (160 days after treatment) and analysed. TRR levels of 0.69–0.70 mg/kg were found in potato tubers. Cadusafos undergoes initial hydrolysis to the transient butane-2-thiol, which undergoes a series of oxidations and methylations to yield a major product, hydroxy 2-butyl methylsulfone. This compound is further oxidized to two isomers of 1-carboxyhydroxyisopropylmethylsulfone, which, in conjugated form, represent the major metabolites in potato tubers (32–37% TRR, 0.22–0.25 mg/kg).

Field Corn

Metabolism of cadusafos was studied in corn using a 2 kg ai/ha treatment rate. The chemical was applied as a 20% granular formulation in bands to the soil. Corn plants were grown to maturity in the greenhouse. Plant samples were taken at 30 and 60-days post-treatment, at silage, and finally at maturity, i.e., grain and stover. TRR levels ranged from 0.85 mg/kg (cadusafos equivalents) in the 60-day post plant forage, to 2.87 mg/kg in the stover. Grain TRR levels were 0.23 mg/kg cadusafos equivalents found only in the mature (160 day) plant. Cadusafos is not stable in the plant and is degraded to more polar and water soluble metabolites. Specifically, analysis of the 30 day, 60 day, silage, and stover samples showed that cadusafos degrades to 2-butanesulfonic acid, hydroxy-2-butanesulfonic acid, and butanediols. S-2-butyl phosphorothioic acid was a minor metabolite in corn samples, while S,S-di-(2-butyl) phosphorodithioic acid was present only in the 30 and 60 day plant samples at less than 0.01 mg/kg. Further analysis of the organosoluble metabolites showed the presence of methyl 2-butyl sulfone, and hydroxy 2-butyl methylsulfone as minor components. Radiocarbon in the grain was analysed and was found to be primarily due to incorporation into glucose, indicating that the parent chemical undergoes a rapid and facile degradation in the corn plant.

Radish

Cadusafos was applied to soil at a rate of 9 kg ai/ha, and radish seeds were sown in the soil. At 50 days after treatment of [^{14}C]-cadusafos, mature radishes were harvested. The radishes were separated into the roots and the foliage for separate analysis. The recoveries of radioactivity in the root, foliage and soil accounted for 0.3%, 1.0% and 70.9% of the applied radioactivity, respectively. The total radioactive residues (TRRs) in the root, foliage and soil were 1.6 mg/kg, 5.0 mg/kg and 10.7 mg/kg equivalents of cadusafos, respectively.

The radish metabolism study showed that numerous compounds were detected in the extractable fractions from the root. There were no metabolites which were more than 4%TRR (0.07 mg/kg equivalent of cadusafos). The parent compound was detected at 0.8%TRR (0.014 mg/kg) in the root. Numerous compounds were also detected in the extractable fractions from the foliage. All the metabolites were less than 10%TRR or 0.5 mg/kg except for methyl 2-butyl sulfone (19%TRR, 0.88 mg/kg). The parent compound was detected at 0.4% (0.018 mg/kg) in foliage. Many metabolites in the root and foliage were polar compounds which were found in the water-soluble fraction. In the soil no metabolite comprised more than 2%TRR.

Tomato

Radiolabelled cadusafos was applied by drip irrigation to the soil surface on two separate occasions at a total nominal rate of 6 kg ai/ha. The first application was made prior to transplanting at a rate of 4 kg ai/ha with a second 60 days later at 2 kg ai/ha. In tomato plants, cadusafos is metabolised via butane-2-thiol to butane-2-sulfonic acid and numerous minor metabolites and conjugates. Radioactive residues were mainly taken up via the roots into the shoots, whereas the uptake of residues into fruits was low. The TRR in edible tomato fruit ranged between 0.028 to 0.093 mg/kg. Tomatoes were separated into pomace and juice fractions and analysed. It was observed that the

major part of the radioactivity (up to 95%) found in the fruits was present in tomato juice. Analyses of the tomato juice samples showed up to 22 radioactive fractions in addition to the parent compound. All fractions were below 10% TRR, except one fraction, likely consisting of several compounds characterised as conjugates, found in green tomatoes. However, none of the radioactive fractions exceeded 0.010 mg/kg in tomato fruit. The major part of the radioactive residue was shown to be conjugated to sugars.

Environmental fate

The degradation of radiolabelled cadusafos in aerobic conditions was investigated in silt loam and sandy loam soils in the US, and in clay loam and silt loam soils in Germany and Spain. The estimated time to 50% degradation (DT_{50}) ranged from 11–62 days in the reported studies. These studies showed that cadusafos has a relatively short estimated half-life in soil.

To investigate the possible photodegradation of cadusafos in soil, sandy loam soil samples were exposed to natural sunlight (11 hour photo periods per day) following treatment with radiolabelled cadusafos at approximately 1 mg/kg and analysed at standard intervals up to 30 days. After 30 days, only 1% of the applied cadusafos was found to have degraded into three compounds. The slow photochemical degradation is in line with the low UV/visible absorbance of cadusafos. Thus, cadusafos may be considered a photolytically-stable compound.

Buffered aqueous solutions (pH 5, 7. and 9) containing approximately 3 mg/L of radiolabelled cadusafos were analysed for hydrolysis at intervals up to 34 days. Cadusafos was stable at pH 5 and 7 during the 34-day study period. At pH 9, slow hydrolysis was observed. Cadusafos may be considered a hydrolytically-stable compound.

Rotational Crops

No rotational crop studies were submitted for review. For rotated crops there would be no expectation of residues remaining in the soil following early season applications as cadusafos has a relatively short estimated half-life in soil.

Methods of analysis

The Meeting received description and validation data for a single-residue analytical method for cadusafos in samples of plant origin. The method is based on extraction with a methanol/water mixture, gravity filtering though glass wool and partitioning with methylene chloride, followed by liquid-liquid extraction using water and dichloromethane and an additional clean-up on an alumina column. The organic phase was filtered through anhydrous sodium sulfate, concentrated and taken up with hexane. Further clean up was achieved using silicagel SEP PAK cartridges and eluting cadusafos with 25% ethyl acetate in hexane. Quantitative determination of the active substance was performed using gas chromatography and a flame photometric detector operating in phosphorous mode.

The method was validated for banana, potato, melon, green beans, strawberry and peppers with a LOQ of 0.005 mg/kg (0.001 mg/kg for banana). Method recoveries ranged from 80–94% for banana pulp and 87–94% for potatoes, with RSDs < 10%. The method was used in the supervised trials on plant commodities evaluated by this Meeting (banana and potato) with concurrent recoveries within the range of 70–110% and RSD < 10%.

Adequate single-residue methods exist for both gathering data in supervised trials and for monitoring and enforcing cadusafos MRLs in the matrices validated. No information regarding the recovery of cadusafos through multiresidue methods was submitted. However, organophosphate compounds are generally amenable to analysis by multiresidue methods and the Pesticide Data Program of the United States Department of Agriculture has reported monitoring results for cadusafos residues in banana samples.

Stability of pesticide residues in stored analytical samples

The Meeting received information on the stability of cadusafos in freezer-stored samples of banana, potato, and corn. The results show that cadusafos was stable under freezer-storage conditions during the tested storage interval of 14–15 months, which covers the storage intervals in the supervised trials evaluated by this Meeting.

Residue Definition

The plant metabolism studies indicate that significant portions of cadusafos are oxidized and then converted to the corresponding conjugates in plant matrices. However, due to the lower toxicity of the polar conjugates formed, the Meeting concluded that the residue definition for plant commodities for purposes of enforcement is cadusafos. The Meeting also concluded that for purposes of dietary intake considerations, the residue definition is cadusafos alone. This determination is consistent with conclusions of the 2009 JMPR, which listed cadusafos as the only toxicologically significant compound in plants, animals, and the environment.

The octanol-water partition coefficient of cadusafos (log K_{OW} = 3.9) implies that cadusafos is likely to be fat soluble. The Meeting determined there was insufficient information available to reach a conclusion regarding the fat solubility of cadusafos in livestock commodities.

Results of supervised trials on crops

The Meeting received results from supervised trials with cadusafos on banana and potato. All results on relevant commodities in trials conducted according to GAP were less than the method LOQ. Consequently, it was not suitable to use the NAFTA calculator to estimate the maximum residue levels. Instead, maximum residue estimation was based on the method LOQ.

Banana

The Meeting received results from supervised trials with cadusafos used on bananas in Australia, Costa Rica (n = 6), Ecuador, Guatemala, Honduras (n = 2), Ivory Coast (n = 2), Martinique, Mexico, and Philippines (n = 2). The GAP in all these countries (except Ecuador: 2 × 2 g ai/plant) specifies two soil applications at a rate of 3 g ai/plant, or three applications at a rate of 2 g ai/plant, for a total rate of 6 g ai/plant per year, with no retreatment interval (RTI) or pre-harvest interval (PHI) given.

The trials reported cadusafos residues in banana peel and pulp samples over a wide range of PHIs and at several treatment rates. The LOQ for all trials was 0.005 mg/kg except for the trial conducted in the Philippines, where the LOQ was 0.02 mg/kg.

All banana pulp samples had residues < 0.005 mg/kg, except for the Philippines trial, where < 0.02 mg/kg was reported. Similarly, all peel samples were < 0.005 mg/kg, except for the Martinique trial which reported detectable cadusafos levels in peel samples harvested at several PHIs, including a maximum level of 0.022 mg/kg at a 0-day PHI following a single application of 6 g ai/plant; and one trial from Costa Rica where a two peel samples had cadusafos residues at 0.005 mg/kg.

Based on the submitted trials reflecting the GAP, the Meeting estimated a maximum residue level for cadusafos in banana of 0.01 mg/kg to confirm the previous recommendation of 0.01 mg/kg, an STMR of 0.005 mg/kg and an HR of 0.005 mg/kg.

The recommendations are supported by monitoring data results from the USDA's Pesticide Data Program (PDP), which reported no detects in 1393 samples analysed in the years 2001 and 2002, when the LOQ ranged from 0.005–0.025 mg/kg, and no detects in 532 samples analysed in the years 2006 and 2007, when the LOQ was 0.005 mg/kg.

Potato

The Meeting received results from supervised trials with cadusafos used on potato in Brazil, Mexico (3), Spain (3), and Greece (2).

The GAP of Brazil for potato specifies 3 kg ai/ha, 1 application, with a 90-day PHI. One trial in Brazil was conducted at the GAP, including a double rate treatment. Cadusafos residues were < 0.02 mg/kg in both cases.

The GAP of Mexico for potatoes specifies 5 kg ai/ha, 1 application, and a 144-day PHI. Two trials in Mexico were conducted at the GAP rate; a third trial conducted in Mexico reported a PHI of 193 days and, therefore, was not according to GAP. There were two trials conducted in Spain at a double rate. A third Spanish trial reported a residue level of 0.03 mg/kg; however, the PHI was only 88 days in this trial. As no GAP was submitted from Spain or Greece, trials conducted in those countries were not considered further for maximum residue level estimations. At the Mexico GAP, cadusafos residues were: < 0.005 and 0.008 mg/kg.

The Meeting determined that insufficient residue data were available to estimate a maximum residue level for potato. The Meeting therefore agreed to withdraw its previous maximum residue level recommendation of 0.02 mg/kg for potato.

Fate of residues during processing

The Meeting received processing studies for potato. The residue definition recommended for plant commodities will suffice for processed plant commodities (parent only).

The processing (or transfer) factors derived from the processing studies are summarised in the table below. The factors are the ratio of the total residue in the processed commodity divided by the total residue in the raw agricultural commodity (RAC).

Processing (Transfer) Factors from the Processing of Raw Agricultural Commodities (RACs) with Field-Incurred Residues from Foliar Treatment with Cadusafos.

RAC	Processed Commodity	Processing Factor [a]
Potato	Peel [b]	0.6, 0.33, 0.5 Mean: 0.48
	Peeled potato [c]	< 0.5,< 0.2,< 0.33, < 0.25 Mean: < 0.32
	Boiled potato [d]	< 0.5,< 0.2,< 0.33, < 0.25 Mean: < 0.32

[a] Each value represents a separate study. The processing factor is the ratio of the total residue in the processed item divided by the total residue in the RAC.

[b] Peels were from boiled potatoes. In one trial with raw peels, a PF of 7.5× was determined.

[c] Potato with no peel after boiling.

[d] Boiled potato with peel.

No MRLs are appropriate for processed potato commodities.

Estimated maximum and mean dietary burdens of farm animals

There are no cattle or poultry feed items resulting from the RACs for which the 2010 Meeting made maximum residue level recommendations, and hence, no need to calculated dietary burden levels for farm animals.

Animal commodity maximum residue levels

A bovine feeding study was not provided. However, there are no cattle feed items resulting from the RACs for which the 2010 Meeting made maximum residue level recommendations, and hence, no need to recommend maximum residue levels for ruminant commodities.

A poultry feeding study was not provided. However, as there are no poultry feed items resulting from the RACs which the 2010 Meeting evaluated, recommendations for maximum residue levels for poultry commodities were unnecessary.

RECOMMENDATIONS

On the basis of the data from supervised trials the Meeting concluded that the residue levels listed below are suitable for establishing maximum residue limits and for IEDI and IESTI assessments.

Definition of the residue (for compliance with the MRL and for estimation of dietary intake)*: cadusafos*.

Commodity		MRL, mg/kg		STMR or STMR-P, mg/kg	HR, mg/kg
CCN	Name	New	Previous		
FI 0327	Banana	0.01	0.01	0.005	0.005
VR 0589	Potato	W [a]	0.02		

[a] W: the recommendation is withdrawn

DIETARY RISK ASSESSMENT

Long-term intake

The evaluation of cadusafos has resulted in recommendations for MRLs and STMRs for bananas. Bananas were included at the appropriate level in the dietary intake calculations. The International Estimated Daily Intakes (IEDI) for the 13 GEMS/Food regional diets, based on the banana STMR were in the range 0–1% of the maximum ADI of 0.0005 mg/kg bw.

The Meeting concluded that the long-term intake of residues of cadusafos from its use on bananas was unlikely to present a public health concern.

Short-term intake

The International Estimated Short-Term Intake (IESTI) for cadusafos was calculated for bananas. The short term intake of bananas represented 20% of the ARfD of 0.001 mg/kg bw for the general population, and 40% of the ARfD of 0.001 mg/kg bw for children ≤ 6 years. Accordingly, the Meeting concluded that the short-term intake of residues of cadusafos from its use on bananas was unlikely to present a public health concern.

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