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HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate E – Food Safety: plant health, animal health and welfare, international questions
E1 - Plant health

Flufenacet

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COMMISSION WORKING DOCUMENT - DOES NOT NECESSARILY REPRESENT THE VIEWS OF THE COMMISSION SERVICES

Review report for the active substance **flufenacet**

Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 4 July 2003 in view of the inclusion of flufenacet in Annex I of Directive 91/414/EEC.

1. Procedure followed for the evaluation process

This review report has been established as a result of the evaluation of the new active substance flufenacet, made in the context of the work provided for in Articles 5 and 6 of Directive 91/414/EEC concerning the placing of plant protection products on the market, with a view to the possible inclusion of this substance in Annex I to the Directive.

In accordance with the provisions of Article 6(2) of Directive 91/414/EEC, the French authorities received on 1 February 1996 an application from Bayer AG (now Bayer CropScience), hereafter referred to as the applicant, for the inclusion of the active substance flufenacet in Annex I to the Directive. French authorities indicated to the Commission on 25 October 1996 the results of a first examination of the completeness of the dossier, with regard to the data and information requirements provided for in Annex II and, for at least one plant protection product containing the active substance concerned, in Annex III to the Directive. Subsequently, and in accordance with the requirements of Article 6(2), a dossier on flufenacet was distributed to the Member States and the Commission.

The Commission referred the dossier to the Standing Committee on Plant Health in the meeting of the working group 'legislation' thereof on 19 December 1996, during which the Member States confirmed the receipt of the dossier.

In accordance with the provisions of Article 6(3), which requires the confirmation at Community level that the dossier is to be considered as satisfying, in principle, the data and information requirements provided for in Annex II and, for at least one plant protection product containing the active substance concerned, in Annex III to the Directive and in accordance with the procedure laid

down in Article 20 of the Directive, the Commission confirmed in its Decision 97/362/EC[1] of 21 May 1997 that these requirements were satisfied.

Within the framework of that decision and with a view to the further organisation of the works related to the detailed examination of the dossier provided for in Article 6(2) and (4) of Directive 91/414/EEC, it was agreed between the Member States and the Commission that France would, as rapporteur Member State, carry out the detailed examination of the dossier and report the conclusions of its examination accompanied by any recommendations on the inclusion or non-inclusion and any conditions relating thereto, to the Commission as soon as possible and at the latest within a period of one year.

France submitted to the Commission on 6 January 1998 the report of its detailed scientific examination, hereafter referred to as the draft assessment report, including, as required, a recommendation concerning the possible inclusion of flufenacet in Annex I to the Directive.

On receipt of the draft assessment report, the Commission forwarded it for consultation to all the Member States as well as to the sole applicant on 25 March 1998.

The Commission organised further an intensive consultation of specialised scientific experts from a representative number of Member States, to review the draft assessment report and the comments received thereon (peer review), in particular on each of the following disciplines :

- identity and physical /chemical properties ;
- fate and behaviour in the environment ;
- ecotoxicology ;
- mammalian toxicology ;
- residues and analytical methods ;
- regulatory questions.

The meetings for this consultation were organised on behalf of the Commission by the Biologische Bundesanstalt für Land und Forstwirtschaft (BBA) in Braunschweig, Germany, from September 1998 to January 1999.

The report of the peer review (i.e. full report) was circulated, for further consultation, to Member States and the sole applicant on 18 May 1999.

The dossier, draft assessment report and the peer review report (i.e. full report) including in particular an outline resumé of the remaining technical questions, were referred to the Standing Committee on the Food Chain and Animal Health, and specialised working groups of this Committee, for final examination, with participation of experts from the 15 Member States. This final examination took place from December 2001 to July 2003, and was finalised in the meeting of the Standing Committee on 4 July 2003.

The present review report contains the conclusions of this final examination; given the importance of the draft assessment report, the peer review report (i.e. full report) and the comments and clarifications submitted after the peer review as basic information for the final examination process,

[1] OJ No L152, 11.06.1997, p.31.

these documents are considered respectively as background documents A, B and C to this review report and are part of it.

These documents were also submitted to the Scientific Committee for Plants for separate consultation. The Committee was asked to comment on two degradation products (M2 and M4) of the active substance, which were detected in lysimeters leachates, and on the exposure of operators. In its opinion[2] the Committee found for the M2 and M4 metabolites that the risk to non-target terrestrial organisms were not yet adequately assessed and also identified other degradation products for which the risk to non-target organisms needed further evaluation. The Committee was of the opinion that operator risk assessment of flufenacet has been adequately addressed but noted that the sensitising potential of the formulation deserves proper attention. The missing assessments were subsequently provided by the Rapporteur and evaluated in the working group of the Standing Committee.

2. Purposes of this review report

This review report, including the background documents and appendices thereto, have been developed and finalised in support of the Directive **2003/84/EC**[3] concerning the inclusion of flufenacet in Annex I to Directive 91/414/EEC, and to assist the Member States in decisions on individual plant protection products containing flufenacet they have to take in accordance with the provisions of that Directive, and in particular the provisions of article 4(1) and the uniform principles laid down in Annex VI.

This review report provides also for the evaluation required under Section A.2.(b) of the above mentioned uniform principles, as well as under several specific sections of part B of these principles. In these sections it is provided that Member States, in evaluating applications and granting authorisations, shall take into account the information concerning the active substance in Annex II of the directive, submitted for the purpose of inclusion of the active substance in Annex I, as well as the result of the evaluation of those data.

In parallel with the provisions of Article 7(6) of Regulation 3600/92 for existing active substances, the Commission and the Member States will keep available or make available this review report for consultation by any interested parties or will make it available to them on their specific request. Moreover the Commission will send a copy of this review report (not including the background documents) to the applicant.

The information in this review report is, at least partly, based on information which is confidential and/or protected under the provisions of Directive 91/414/EEC. It is therefore recommended that this review report would not be accepted to support any registration outside the context of Directive 91/414/EEC, e.g. in third countries, for which the applicant has not demonstrated possession of regulatory access to the information on which this review report is based.

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[2] Opinion of the Scientific Committee on Plants on specific questions from the Commission concerning the evaluation of flufenacet [FOE 5043] in the context of Council Directive 91/414/EEC - SCP/FLUFEN/002-Final adopted 17 October 2001

[3] OJ No L 247, 30.09.2003, p.20.

3. Overall conclusion in the context of Directive 91/414/EEC

The overall conclusion from the evaluation is that it may be expected that plant protection products containing flufenacet will fulfil the safety requirements laid down in Article 5(1)(a) and (b) of Directive 91/414/EEC. This conclusion is however subject to compliance with the particular requirements in sections 4, 5, 6 and 7 of this report, as well as to the implementation of the provisions of Article 4(1) and the uniform principles laid down in Annex VI of Directive 91/414/EEC, for each flufenacet containing plant protection product for which Member States will grant or review the authorisation.

Furthermore, these conclusions were reached within the framework of the following uses which were proposed and supported by the sole submitter:

- herbicide against annual grass weeds in cereals, corn, soybeans and sunflower with a maximum application rate of 0.6 kg / ha.

Extension of the use pattern beyond those described above will require an evaluation at Member State level in order to establish whether the proposed extensions of use can satisfy the requirements of Article 4(1) and of the uniform principles laid down in Annex VI of Directive 91/414/EEC.

4. Specific conclusions which are highlighted in this evaluation

4.1 Residues of flufenacet in foodstuffs

The review has established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health. The Theoretical Maximum Daily Intake (TMDI) for a 60 kg adult is 8 % of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet (August 1994). Estimates of acute dietary exposure of adults and toddlers do not exceed the Acute Reference Dose (ARfD).

4.2 Exposure of operators, workers and bystanders

The review has identified acceptable exposure scenarios for operators, workers and bystanders, which require, however, confirmation for each plant protection product in accordance with the relevant sections of the above mentioned uniform principles.

4.3 Ecotoxicology

The review has also concluded that under the proposed and supported conditions of use there are no unacceptable effects on the environment, as provided for in Article 4 (1) (b) (iv) and (v) of Directive 91/414/EEC, provided that certain conditions are taken into account as detailed in section 7 of this report.

5. Identity and Physical/chemical properties

The main identity and the physical/chemical properties of flufenacet are given in Appendix I.

The active substance shall have a minimum purity of 950 g/kg technical product (based on commercial plant production)

The review has established that for the active substance notified by the applicant, none of the manufacturing impurities considered are, on the basis of information currently available, of toxicological or environmental concern.

6. Endpoints and related information

In order to facilitate Member States, in granting or reviewing authorisations, to apply adequately the provisions of Article 4(1) of Directive 91/414/EEC and the uniform principles laid down in Annex VI of that Directive, the most important endpoints as identified during the evaluation process are listed in Appendix II.

7. Particular conditions to be taken into account on short term basis by Member States in relation to the granting of authorisations of plant protection products containing flufenacet

On the basis of the proposed and supported uses, the following particular issues have been identified as requiring particular and short term attention from the Member States, in the framework of any authorisations to be granted, varied or withdrawn, as appropriate:

Member States

- should pay particular attention to the protection of algae and aquatic plants.
- should pay particular attention to the potential for groundwater contamination, when the active substance is applied in regions with vulnerable soil and/or climatic conditions.
- should pay particular attention to the protection of operators.

Risk mitigation measures must be applied, where appropriate.

8. List of studies to be generated

No further studies were identified which were considered at this stage, and under the current inclusion conditions necessary in relation to the inclusion of flufenacet in Annex I.

However, to support authorisations for use under certain conditions, some endpoints may still require the generation of additional studies to be submitted to the Member States. This may particularly be the case for:

- Additional studies on analytical methods concerning impurities and the metabolite M2;
- Additional, confirmatory data on the effects on earthworms, in particular when high use rates are applied.

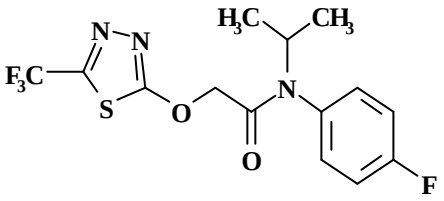
9. Updating of this review report

The technical information in this report may require periodic updating to take account of technical and scientific developments as well as of the results of the examination of any information referred to the Commission in the framework of Articles 7, 10 or 11 of Directive 91/414/EEC. Such adaptations will be examined and finalised in the Standing Committee on the Food Chain and Animal Health, in connection with any amendment of the inclusion conditions for flufenacet in Annex I of the Directive.

APPENDIX I

Identity, physical and chemical properties

FLUFENACET

Common name (ISO)	Flufenacet
Development Code	FOE 5043
Chemical name (IUPAC)	4'-fluoro-*N*-isopropyl-2-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yloxy]acetanilide
Chemical name (CA)	N-(4-fluorophenyl)-N-(1-methylethyl)-2-[[5-(trifluoromethyl)-1, 3, 4-thiadiazol-2-yl]oxy]acetamide
CIPAC No	588
CAS No	142459-58-3
EEC No	Not available
FAO SPECIFICATION	Not available
Minimum purity	950 g/kg
Molecular formula	$C_{14}H_{13}F_4N_3O_2S$
Molecular mass	363.34
Structural formula	

Melting point	Partial melting point at 76 °C. Melting point of the new crystals at 79 °C.
Boiling point	Not measurable, decomposition above 150 °C
Appearance	White solid with chalk-like odour (purity 93.4 %)
Relative density	1.45 at 20 °C
Vapour pressure	$9 \cdot 10^{-5}$ Pa at 20 °C (N-isomer)
Henry's law constant	$9 \cdot 10^{-4}$ $Pa \cdot m^3 \cdot mol^{-1}$
Solubility in water	At 20 °C: pH 4 : 56 mg/l pH 7 : 56 mg/l pH 9 : 53 mg/l
Solubility in organic solvents	At 25 °C: acetone: >200 g/l acetonitrile: >200 g/l toluene: >200 g/l dichloromethane: >200 g/l hexane: 8.7 g/l propanol: 170 g/l n-octanol: 88 g/l dimethylformamide: >200 g/l dimethylsulfoxide: >200 g/l propylene glycol: 74 g/l
Partition co-efficient (log P_{OW})	3.2
Hydrolytic stability (DT_{50})	At 20 °C: pH 5 : 14835 d pH 7 : 1547 d pH 9 : 654 d
Dissociation constant	No dissociation constant
Quantum yield of direct photo-transformation in water at e >290 nm	λ max : 210 nm No absorption >210-410 nm
Flammability	Not flammable
Explosive properties	Not explosive
UV/VIS absorption (max.)	λ max : 210 nm No absorption > 210 - 410 nm
Photostability in water (DT_{50})	Stable

APPENDIX II

END POINTS AND RELATED INFORMATION

FLUFENACET

1 Toxicology and metabolism

Absorption, distribution, excretion and metabolism in mammals

Rate and extent of absorption:	Rapidly, 75 to 94 % based on urine and tissue distribution
Distribution:	Widely distributed
Potential for accumulation:	No potential for accumulation
Rate and extent of excretion:	More than 90 % excreted via urine, feces and air in 72 h (considerable entero-hepatic recirculation).
Toxicologically significant compounds:	Parent compound and thiadone metabolite
Metabolism in animals:	Extensive metabolism. Cleavage of the molecule, glutathione conjugation of the aryl-acetamide moiety, degradation of the thiadiazole ring.

Acute toxicity

Rat LD_{50} oral:	589 mg/kg bw (females), 1617 mg/kg bw (males)
Rat LD_{50} dermal:	> 2000 mg/kg bw
Rat LC_{50} inhalation:	> 3.74 mg/l
Skin irritation:	Non-irritant
Eye irritation:	Non-irritant
Skin sensitization (test method used and result):	Sensitising (M & K)

Short term toxicity

Target / critical effect:	Liver, thyroid, kidney; eye and nervous system (dog only)
Lowest relevant oral NOAEL / NOEL:	50 ppm (1.67 mg/kg bw/d; 90-d & 1-y dog)
Lowest relevant dermal NOAEL / NOEL:	20 mg/kg bw/d (21-d rat)
Lowest relevant inhalation NOAEL / NOEL:	No data, not required

Genotoxicity

No genotoxic potential

Long term toxicity and carcinogenicity

Target / critical effect:	Liver, thyroid, eye, kidney
Lowest relevant NOAEL:	No NOAEL identified LOEL: 25 ppm (1.2 mg/kg bw/d; 2-y rat), based on increased incidence of renal pelvic mineralisation
Carcinogenicity:	No carcinogenic potential

Reproductive toxicity

Target / critical effect - Reproduction:	No reproductive toxic effects
Lowest relevant reproductive NOAEL / NOEL:	500 ppm (37.4 mg/kg bw/d) – 2 generation rat
Target / critical effect - Developmental toxicity:	Reduced fetal weight and skeletal variations at maternal toxic doses
Lowest relevant developmental NOAEL / NOEL:	25 mg/kg bw/d (rat, rabbit)

Delayed neurotoxicity

Neurotoxic effects in rats after acute and subchronic exposure; NOEL 7.3 mg/kg bw/d (rat, 90d study). Thiadone seems to be a neurotoxic metabolite in dogs.

Other toxicological studies

Mechanistic studies showing increased hepatic T4 metabolism in rats

Medical data

No data, new compound

Summary

	Value	Study	Safety factor
ADI:	0.005 mg/kg bw/d	rat: 2y study (LOEL)	250
AOEL systemic:	0.017 mg/kg bw/d	dog: 90d and 1y study	100
AOEL inhalation:	Not required		
AOEL dermal:	Not required		
ARfD (acute reference dose):	0.017 mg/kg bw/d	dog: 90d and 1y study	100

Dermal absorption

In vitro dermal absorption in human M/L: undiluted with FOE 5043 60WG: 10 % S: diluted with FOE 5043 60WG: 60%

2 Fate and behaviour in the environment

2.1 Fate and behaviour in soil

Route of degradation

Aerobic:

Mineralization after 100 days:	10.2 - 20.8 % [fluorophenyl-UL-^{14}C]FOE 5043 31.9 % [thiadiazole-2-^{14}C]FOE 5043 (90 d)
Non-extractable residues after 100 days:	29.9 - 56.2 % [fluorophenyl-UL-^{14}C]FOE 5043 6.0 % [thiadiazole-2-^{14}C]FOE 5043 (90 d)
Major metabolites above 10 % of applied active substance: name and/or code % of applied rate (range and maximum)	FOE sulfonic acid : 13.5 - 26.3 % (100 d) FOE oxalate: 6.6 - 15.6 % (28 d)

Supplemental studies

Anaerobic:	No data provided, not required (field studies)
Soil photolysis:	Not significant
Remarks:	None

Rate of degradation

Laboratory studies

DT_{50}lab (20 °C, aerobic):

Soil type	pH	OC (%)	DT_{50} (days)
loamy sand	6.2	2.58	39
silt loam	7.3	0.9	15
silt loam	5.8	2.4	27
sandy loam*	6.2	0.32	34-64 (mean 48)

* 2 labels, 21° C, 75 % FC

FOE sulfonic acid

Soil type	pH	OC (%)	DT_{50} (days)
sand	5.3	0.57	270
loamy sand	6.3	2.48	189
silt loam	7.3	0.9	247

FOE oxalate (estimated from parent study)

Soil type	pH	OC (%)	DT_{50} (days)
loamy sand	6.2	2.58	5
silt loam I	7.3	0.9	17
silt loam II	5.8	2.4	12

DT_{90}lab (20 °C, aerobic):

Soil type	pH	OC (%)	DT_{90} (days)
loamy sand	6.2	2.58	130
silt loam	7.3	0.9	52
silt loam	5.8	2.4	92

DT_{50}lab (10 °C, aerobic):

86 d (from DT_{50} 39 d at 20° C, using Q_{10} 2.2)

DT_{50}lab (20 °C, anaerobic):

No data provided, not required

Field studies (country or region)

DT_{50f} from soil dissipation studies:

DT_{50f}: Germany (4 sites, bare soil), Northern France (2 sites, crop), Southern France (2 sites, crop), Italy (2 sites, crop). LOD 10 µg/kg (< 6 %)

Location	Autumn (240 g/ha)	Early spring (240 g/ha)	Spring (480-600 g/ha)
Germany	38-43 d	-	15-54-31-53 d
N. France	-	13-16 d	16-38 d
S. France	-	-	30-36-34-42 d
Italy	-	-	38-48 d

Metabolites not detected above LOD

DT_{90f} from soil dissipation studies:

DT_{90f}: same conditions as for DT_{50f}

Location	Autumn (240 g/ha)	Early spring (240 g/ha)	Spring (480-600 g/ha)
Germany	125-144 d	-	51-178-101-177 d
N. France	-	43-52 d	177-198 d
S. France	-	-	98-120-112-139 d
Italy	-	-	126-158 d

Soil accumulation studies:

Not relevant

Soil residue studies:

Not relevant

Remarks:

None

Adsorption/desorption

K_f / K_{OC}:

Soil type	pH	OC (%)	Koc	slope
silt loam	5.9	1.68	190	0.84
clay loam	6.4	1.28	211	0.90
loamy sand	6.4	0.23	696	0.87
sand	5.0	0.17	588	0.98
sandy loam	6.4	1.4	354	0.89
loam	7.1	4.3	113	0.96
silt loam	7.3	2.8	144	0.86

mean Koc 202 (for OC > 0.23 %)

no pH dependence

K_d

pH dependence:

Soil type	pH	OC (%)	oxalate		sulfonic acid	
			Koc	slope	Koc	slope
sand	5.8	0.27	23	1.42	19	0.86
sandy loam	6.3	0.75	13	0.93	15	1.00
silty clay loam	6.6	2.13	7	0.82	10	0.93
silty clay	6.0	1.21	13	0.98	6	1.18
mean (for OC > 0.27 %)			11		10	

Mobility

Laboratory studies:

Column leaching:

No data provided, not required

Aged residue leaching:

2 sand soils (pH 6-6.2, OC 0.26-0.32 %)

Radioactivity in leachates (%)		
Incubation	30 days	90 days
Total	< 30 %	< 44 %
Parent	< 16 %	< 0.3 %
FOE oxalate (M1)	< 6.7 %	< 27 %
FOE sulfonic acid (M2)	< 10.1 %	< 10.9 %
FOE thioglycolate sulfoxide (M4)	< 6.2	< 3.6
Others	< 1.6 %	< 2.9 %

Field studies:

Lysimeter/Field leaching studies:	Lysimeter (sandy loam soil, < 1.41 % OC) <u>corn/corn rotation</u> (2 x 480 g a.s./ha) Total mean 0.87-0.99 µg/l, max. 2.23 µg/l (y 1) mean 0.46-0.67 µg/l, max. 1.0 µg/l (y 2) mean 0.23-0.33 µg/l, max. 0.33 µg/l (y 3) a.s. < 0.035 µg/l FOE oxalate < 0.04 µg/l FOE thioglycolate < 0.08 µg/l FOE sulfonic acid mean 0.49-0.59 µg/l, max. 1.29 µg/l (y 1) mean 0.15-0.24 µg/l (y 2) <u>corn/wheat rotation</u> (480 + 180 g a.s./ha) Total mean 2.5 µg/l, max. 5 µg/l (year 1) mean 0.24 µg/l (year 2) a.s. not identified FOE oxalate and thioglycolate < 0.1 µg/l FOE sulfonic acid : mean 1.49 µg/l, max. 3.7 µg/l (year 1) mean 0.015 µg/l (year 2)
Remarks:	None

2.2 Fate and behaviour in water

Abiotic degradation

Hydrolytic degradation:	pH 5 (25° C): DT_{50} > 1 year pH 7 (25° C): DT_{50} > 1 year pH 9 (25° C): DT_{50} > 1 year
Major metabolites:	none
Photolytic degradation:	Not significant (DT_{50} > 1 year)
Major metabolites:	none

Biological degradation

Readily biodegradable:	Not readily biodegradable
Water/sediment study:	
DT_{50} water:	46.3 - 61.7 d [fluorophenyl-^{14}C] FOE 5043 (1st order)
DT_{90} water:	154-205 d
DT_{50} whole system:	76.4-84.6 d (fluorophenyl), 20-31 d (thiadiazole)
DT_{90} whole system:	254-281 d (fluorophenyl), 67-104 d (thiadiazole)
Distribution in water / sediment systems (active substance)	max. 34.2 % in sediment (30 d)
Distribution in water / sediment systems (metabolites)	FOE methylsulfide: max. 8 % in water, 3.4 % in sediment on day 157. Thiadone max. 82 % in water (55 d)
Accumulation in water and/or sediment:	Not relevant

Degradation in the saturated zone

No data provided, not required

Remarks: None

2.3 Fate and behaviour in air

Volatility

Vapour pressure:	$9 \cdot 10^{-5}$ Pa at 20 °C (N-isomer)
Henry's law constant:	$9 \cdot 10^{-4}$ $Pa \cdot m^3 \cdot mol^{-1}$

Photolytic degradation

Direct photolysis in air:	No data provided, not required (no absorbance above 290 nm)
Photochemical oxidative degradation in air DT_{50}:	4.7 h (according to Atkinson)
Volatilisation:	from plant surfaces: no data, not required from soil: up to 29 % within 1 day

Remarks:	None

3 Ecotoxicology

Terrestrial Vertebrates

Acute toxicity to mammals:	LD50 (female rat) = 589 mg /kg bw
Acute toxicity to birds:	LD50 (bobwhite quail) = 1608 mg /kg bw
Dietary toxicity to birds:	LC50 (mallard duck) > 4970 ppm
Reproductive toxicity to birds:	NOEC (mallard duck) = 88 ppm
Short term oral toxicity to mammals:	NOEL = 97.5 ppm

Aquatic Organisms

Acute toxicity fish:	LC50 = 2.13 mg /l (96 h; *Lepomis macrochirus*) LC50 > 86.7 mg flufenacet-sulfonic acid /l (96 h; *Oncorhynchus mykiss*) LC50 = 9.1 mg thiadone /l (96 h; *O. mykiss*)
Long term toxicity fish:	NOEC = 0.2 mg/l (97 d; *O. mykiss*)
Bioaccumulation fish:	BCF = 71.4
Acute toxicity invertebrate:	EC50 = 30.9 mg /l (48 h; *Daphnia magna*) EC50 > 87.3 mg flufenacet-sulfonic acid /l (48 h; *D. magna*) EC50 = 31.7 mg thiadone/l (48 h, *D. magna*)
Chronic toxicity invertebrate:	NOEC = 3.26 mg /l (21 d; *D. magna*)
Acute toxicity algae:	EbC50 = 0.00204 mg/l (72 h; *Selenastrum capricornutum*) ErC50 > 86.7 mg flufenacet-sulfonic acid /l (120 h; *Scenedesmus subspicatus*) EbC50 = 4.1 mg thiadone /l (72 h, *S. capricornutum*) ErC50 = 83.8 mg flufenacet-methylsulfide /l (96 h, *S. capricornutum*)
Chronic toxicity sediment dwelling organism:	not relevant
Acute toxicity aquatic plants:	EC50 = 0.00243 mg /l (14 d; *Lemna gibba*) EC50 > 86.7 mg flufenacet-sulfonic acid /l (14 d; *L. gibba*)
Aquatic Indoor Microcosm	NOEC = 0.012 mg a.s./l (WG 60, macophyte, duckweed and periphyton)

Honeybees

Acute oral toxicity:	LD50 > 170 µg /bee
Acute contact toxicity:	LD50 > 194 µg /bee

Other arthropod species

	% Effect
A. rhopalosiphi	Mortality, parasitism, fecundity: > 30 % (adults, WG60, 0.6 kg a.s./ha)
A. rhopalosiphi (extended laboratory test)	Fecundity: < 30 % (adults, WG60, 0.6 kg a.s./ha)
T. pyri	Mortality, reproduction: 100 % (0.6 kg a.s./ha), no effect (5% drift) (protonymphs, WG62.5 [1])
P. cupreus	Mortality, behaviour, feeding activity: no effect (adults, WG60, 0.6 kg a.s./ha)
P. agrestis	Mortality, behaviour, feeding activity: no effect (adults, WG60, 0.6 kg a.s./ha)
A. bilineata	Mortality, behaviour, feeding activity: no effect (adults, WG60, 0.6 kg a.s./ha)
C. septempunctata	Reproduction: no effect (larvae, WG60, 0.6 kg a.s./ha)

[1] 60% flufenacet and 2.6% metosulam

Earthworms

Acute toxicity:	LC50 = 219 mg /kg soil LC50 > 1000 mg flufenacet-sulfonic acid, Na salt /kg soil LC50 > 1000 mg flufenacet oxalate /kg soil
Reproductive toxicity:	NOEC > 4 mg /kg soil

Soil micro-organisms

Nitrogen mineralization:	0.8 and 4 mg /kg soil: no significant effect
Carbon mineralization:	0.8 and 4 mg /kg soil: no significant effect

APPENDIX III

FLUFENACET

List of studies which were submitted during the evaluation process and were not cited in the draft assessment report:

B.1 Identity
B.2 Physical and chemical properties
B.3 Data on application and further information
B.4 Proposals for classification and labelling
B.5 Methods of analysis

Annex point / reference number	**Author(s)**	**Year**	**Title** **Source** **Company, Report No.** **GLP or GEP status** **Published or not**
AII; 1.11 /02	Harbin, D.N.	1998	The composition of technical BAY FOE 5043 Generated by: Bayer Corporation, Submitted by: Bayer AG, Bayer file No.: 108408 Date: May 18, 1998 GLP not published
AII; 4.1 /03	Leibowitz, S.J.	2000	HPLC Determination of Impurities in BAY FOE 5043 Generated by: Bayer Corporation, Submitted by: Bayer AG, Bayer file No.: TM: C-16.03-02 Date: March 29, 2000 GLP not published
AII; 4.1 /04	Smead, C.F.	1999	HPLC Determination of Impurities in Flufenacet Generated by: Bayer Corporation, Submitted by: Bayer AG, Bayer file No.: TM: C-16.01-03 Date: July 13, 1999 GLP not published
AII; 4.1 /05	Harbin, D.N.	1997	Validation of test method C-16.01: Quantitation of BAY FOE 5043 in technical material and 60% dry flowable formulations Generated by: Bayer Corporation, Submitted by: Bayer AG, Bayer file No.: 107584 Date: April 11, 1997 GLP not published

Annex point / reference number	**Author(s)**	**Year**	**Title** **Source** **Company, Report No.** **GLP or GEP status** **Published or not**
AII; 4.1 /06	Harbin, D.N.	1998	The composition of technical BAY FOE 5043 Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: 108408 Date: May 18, 1998 GLP not published
AII; 4.2.1 /04	Seym, M	1994	Independent laboratory validation of the residue analytical method for FOE 5043 residues in plant Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: 106907 Date: June 24, 1994 GLP not published
AII; 4.2.1 /05	Seym, M.	1998	Multi-residue method for FOE 5043 and its metabolites for plant material Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: MR-840/98 Date: November 6, 1998 non-GLP not published
AII; 4.2.2 /02	Leimkühler, W.M. and Moore, K.S.	1994	Analytical Method for the determination of FOE 5043 and two metabolites in soil Generated by: Miles Inc., Submitted by: Bayer AG, Bayer file No.: 105167 Date: February 10, 1994 GLP not published
AII; 4.2.2 /03	Mattern, G.C.; Parker, G.D.; Leimkühler, W.M.; and Moore K.S.	1994	Analytical method for the determination of FOE 5043 and it`s oxalate, alcohol and methyl sulfoxid metabolites in soil Generated by: Miles Inc., Submitted by: Bayer AG, Bayer file No.: 106242 Date: February 14, 1994 GLP not published
AII; 4.2.3 /02	König, T.	1997	Method for the determination of FOE 5043 in drinking water by HPLC with on-line solid phase extraction Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: MR-473/97, method No. 00489 Date: September 9, 1997 GLP not published

Annex point / reference number	**Author(s)**	**Year**	**Title** **Source** **Company, Report No.** **GLP or GEP status** **Published or not**
AII; 4.2.3 /03	König, T.	1998	Amendment to method 00489, MR-473/97 Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: MR-012/98 Date: March 13, 1998 GLP not published
AII; 4.2.3 /04	Brumhard, B.	1998	Method for the determination of FOE 5043 in surface water by HPLC-MS/MS with solid phase extraction Method 00530 Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: MR-477/98 Date: December 4, 1998 GLP not published
AII; 4.2.3 /05	Brumhard, B.	1999	Method for the determination of FOE 5043 in surface water by HPLC/UV with on-line solid phase extraction Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: MR-764/97 Date: January 15, 1999 GLP not published
AII; 4.2.5 /02	Bajzk, M.E.	1995	Independent laboratory validation of the analytical method for the determination of FOE 5043 in animal matrices Generated by: Miles Inc., Submitted by: Bayer AG, Bayer file No.: 106913 Date: March 22, 1995 GLP not published
AIII; 2.1	Heß, T.	1997	Characterization of a WG-Formulation – FOE 5043 WG 60 (AB 0158162) Generated by: Bayer AG Submitted by: Bayer AG, Bayer file No.: 141005009 Date: Jan. 27, 1997 GLP not published
AIII; 2.4.2	Heß, T.		⇒ *AIII; 2.1*
AIII; 2.6.2	Heß, T.		⇒ *AIII; 2.1*
AIII; 2.8.6.1	Heß, T.		⇒ *AIII; 2.1*

Annex point / reference number	Author(s)	Year	Title Source Company, Report No. GLP or GEP status Published or not
AIII; 2.8.6.2	Heß, T.		⇒ *AIII; 2.1*
AIII; 2.8.6.3	Grohs, R.	1997	Attrition restistance of FOE 5043 WG 60 Generated by: Bayer AG Submitted by: Bayer AG, Bayer file No.: MO-00-000735 Date: Nov. 2, 1999 non-GLP not published
AIII; 4.2 /1		1998	Effective container cleaning for crop protection products ECPA, Brussels Doc.: D 98/NM 3337 Date: Sept. 10, 1998 non-GLP published
AIII; 4.2 /2		1997	Container management strategy ECPA, Brussels Doc.: D/97/NM/730 Date: August 1997 non-GLP published

B.6 Toxicology and metabolism

Annex point / reference number	Author(s)	Year	Title Source Company, Report No. GLP or GEP status Published or not
AII, 5.8.1 /01	Herbold, B.	2000	FOE 5043-sulfonic-acid - Samonella/microsome test plate incorporation and preincubation method Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: PH 29473 Date: January 19, 2000 GLP not published

Annex point / reference number	**Author(s)**	**Year**	**Title** **Source** **Company, Report No.** **GLP or GEP status** **Published or not**
AII, 5.8.1 /02	Krötlinger, F. and Schmidt, U.	2000	FOE 5043 sulfonic acid Plasmakinetics and excretion in urine in a rat study with single oral versus intravenous administration Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: PH 30052 Date: July 25, 2000 GLP not published
AII, 5.8.1 /03	Heimann, K.-G. and Klammroth, E.	2000	Assessment of the toxicological significance of metabolite M4 (thioglycolate sulfoxide) Generated by: Bayer AG, Submitted by: Bayer AG, Date: February 3, 2000 GLP not published
AII, 5.8.1 /04	Herbold, B.	2000	FOE 5043-Thioglycolate Sulfoxide - Salmonella/microsome test - plate incorporation and preincubation method Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: PH 29871 Date: May 12, 2000 GLP not published
AIII; 7.2 /1	Maasfeld, W.	2000	Assessment of operator exposure when applying Flufenacet containing products Generated by: Bayer AG Submitted by: Bayer AG, Bayer file No.: MO-00-006539 Date: Feb. 24, 2000 non-GLP not published
AIII; 7.3	van de Sandt, J.J.M.	1999	In vitro percutaneous absorption of [phenyl-UL-14C]FOE 5043 60 WG through rat and human epidermal membranes Source: TNO; Appeldoorn, NL Generated by: Bayer AG Submitted by: Bayer AG, Bayer file No.: HM 901 Date: Nov. 9, 1999 GLP not published

B.7 Residue data

Annex point / reference number	Author(s)	Year	Title Source Company, Report No. GLP or GEP status Published or not
AII, 6.6 /03	Krolski, M.E.	1997	FOE 5043 60 DF – Magnitude of the residue in field rotational crops Generated by: Bayer Corporation, Submitted by: Bayer AG, Bayer file No.: 107703 Date: March 27, 1997 GLP not published

B.8 Environmental fate and behaviour

Annex point / reference number	Author(s)	Year	Title Source Company, Report No. GLP or GEP status Published or not
AII 7.1.1	Schafer H.	1995	Calculation of DT-50 values of two metabolites of FOE 5043 in soil under aerobic conditions Bayer A.G., report MR-1085/95
AII 7.1.1	Schafer H.	1998	Amendment to Report MR-1085/95 Bayer A.G., report MR-037/98
AII; 7.1.3 /09	Hellpointner, E.	1997	Lysimeter study on the translocation of FOE 5043 into the subsoil after 2-year use as pre-emergence herbicide in corn Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: PF-4188 (MR-074/97) Date: September 19, 1997 GLP not published
AII; 7.2.1 /07	Halarnkar, P.P. and Irwin, D.W.	1997	Aerobic aquatic metabolism of [Thiadiazole-2-14C]FOE 5043 in two water/sediment systems Generated by: Bayer Corporation, Submitted by: Bayer AG, Bayer file No.: 107822 Date: October 6, 1997 GLP not published

Annex point / reference number	Author(s)	Year	Title Source Company, Report No. GLP or GEP status Published or not
AIII 9.2	Schafer H.	2002	Predicted Environmental Concentrations of FOE5043 and its Metabolites FOE5043 Oxalate and FOE5043 Sulfonic Acid in Ground Water Recharge Based on FOCUS-PELMO. Use in Winter Cereals, Maize, Potatoes, Sunflowers and Soybeans in Europe. Bayer A.G., report MR-119/02

B.9 Ecotoxicology

Annex point / reference number	Author(s)	Year	Title Source Company, Report No. GLP or GEP status Published or not
AII; 8.2.1 /04	Leimkühler, W.M. and Moore, K.S.	1994	Identification of radioactive residues of phenyl-[^{14}C]FOE 5043 in Bluegill Sunfish (*Lepomis macrochirus*) Generated by: Miles Inc., Submitted by: Bayer AG, Bayer file No.: 106577 Date: July 14, 1994 GLP not published
AII; 8.2.6 /04	Anderson, J.P.E.	1995	Range Finding Test: Influence of FOE 5043 T on the Growth of the Green Alga, Selenastrum capricornutum Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: AJO/130095 Date: April 5, 1995 GLP not published
AII; 8.2.6 /05	Anderson, J.P.E.	1997	Growth of the green alga, *Pseudokirchneriella subcapitata* (formerly *Selenastrum capricornutum*), during and after exposure to high concentrations of FOE 5043 Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: AJO/157097 Date: July 14,1997 GLP not published

Annex point / reference number	**Author(s)**	**Year**	**Title** **Source** **Company, Report No.** **GLP or GEP status** **Published or not**
AII; 8.2.6 /06	Dorgerloh, M.	1998	FOE 5043-Methylsulfide -Influence on the Growth of the Green Alga, *Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum)* Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: DOM 98011 Date: June 16, 1998 GLP not published
AII; 8.2.6 /07	Dorgerloh, M.	1998	Toxicity of 14C-FOE 5043 to the Green Alga *Selenastrum capricornutum* Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: DOM 98092 Date: September 9, 1998 originally reported as: Bowers, L.M.: Toxicity of ^{14}C-FOE 5043 to the Green Alga *Selenastrum capricornutum.* Source: Bayer Corp., Kansas, USA; Bayer AG, Report No.: 107114, Date: October 19, 1995 GLP not published
AII; 8.2.6 /08	Hughes, J.S. Alexander, M.M.	1993	Acute toxicity of FOE 5043 (technical) to *Anabaena flos-aquae* Source: Malcolm Pirnie Inc., Tarrytown, NY 10591, USA Generated by: Miles Inc., Submitted by: Bayer AG, Bayer file No.: 105199 Date: December 17, 1993 GLP not published
AII; 8.2.8 /03	Dorgerloh, M.	1998	Acute toxicity of FOE 5043 (technical) to *Lemna gibba* G3 Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: DOM 98091 Date: September 1, 1998 GLP not published originally reported as: Hughes, J.S.; Alexander, M. M.: Acute Toxicity of FOE 5043 (technical) to *Lemna gibba* G3; Source: Miles, Kansas; Bayer AG, Report No.: 105198 Date: December 17, 1993

Annex point / reference number	Author(s)	Year	Title Source Company, Report No. GLP or GEP status Published or not
AII; 8.3.2 /08	Schmuck, R.	1998	Effects of FOE 5043 & DE 511 WG 62.5 on the Life Cycle of the Predaceous Mite (*Typhlodromus pyri*) under Laboratory Conditions Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: Tp 03 Date: October 29, 1998 GLP not published
AII; 8.4.1 /02	Nienstedt, K.M.	1999	FOE 5043-Oxalate: A 14-day acute toxicity test with the earthworm (Eisenia fetida) Source: Springborn Laboratories, Horn, Switzerland Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: 1022.006.630 Date: July 19, 1999 GLP not published
AII; 8.4.1 /03	Nienstedt, K.M.	1999	FOE 5043-Sulfonic acid Na-salt: A 14-day acute toxicity test with the earthworm (Eisenia fetida) Source: Springborn Laboratories, Horn, Switzerland Generated by: Bayer AG, Submitted by: Bayer AG, Bayer file No.: 99-005-1022 Date: July 15, 1999 GLP not published
AII; 8.6 /01	Johns, C.L.	1994	Tier 2 Seed Germination, Seedling Emergence, and Vegetative Vigor Nontarget Phytotoxicity Study Using FOE 5043 Generated by: Miles Inc., Submitted by: Bayer AG, Bayer file No.: 106780 Date: September 14, 1994 GLP not published
AIII; 10.2.2	Foekema, E.M. and Jak, R.G.	1999	The fate and biological effects of flufenacet WG 60 in aquatic indoor microcosms Source: TNO; Appeldoorn, NL Generated by: Bayer AG Submitted by: Bayer AG, Bayer file No.: TNO-MEP-R 99/423 Date: Nov. 29, 1999 GLP not published

APPENDIX IV

List of uses supported by available data

FLUFENACET

Crop and/ Or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max		
Corn	Northern and Southern Europeam Countries	FOE 5043 WG 60	F	Annual grass weeds	WG	60 %	Spray application with standard field sprayers	Pre - emergence	1	-	0.120 – 0.300	200 - 400	0.48 - 0.60	Pre - emergence	-
Soybean, Sunflower	Southern Europeam Countries	FOE 5043 WG 60	F	Annual grass weeds	WG	60 %	Spray application with standard field sprayers	Pre - emergence	1	-	0.120 – 0.300	200 - 400	0.48 - 0.60	Pre - emergence	-
Winter cereals (wheat, rye, barley , triticale)	Northern Europeam Countries	FOE 5043 WG 60	F	Annual grass weeds	WG	60 %	Spray application with standard field sprayers	Early post autumn at the 2nd leaf stage of the grass weeds	1	-	0.030 – 0.120	200 - 400	0.12 - 0.24	2nd leaf stage of the grass weeds	-

Remarks: (a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)

(i) g/kg or g/l

(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997,

(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions