EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

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

Flurtamone
Sanco/10162/2003-Final
3 July 2003

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

Review report for the active substance **flurtamone**

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 flurtamone 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 flurtamone, 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 15 February 1994 an application from Rhône-Poulenc Agro France (now Bayer CropScience), hereafter referred to as the applicant, for the inclusion of the active substance flurtamone in Annex I to the Directive. The French authorities indicated to the Commission on 30 October 1995 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 flurtamone was distributed to the Member States and the Commission.

The Commission referred the dossier to the Standing Committee on the Food Chain and Animal Health in the meeting of the working group 'legislation' thereof on 24 November 1995, 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 1996/341/EC [1] of 20 May 1996 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 21 May 1997 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 flurtamone in Annex I to the Directive.

On receipt of the draft assessment report, the Commission forwarded it for consultation to all the Member States on 18.06.1997 as well as to Rhône-Poulenc Agro France (now Bayer CropScience)being the sole applicant on 26.06.1997.

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 1997 to January 1998.

The report of the peer review (i.e. full report) was circulated, for further consultation, to Member States and the sole applicant on 7 March 1998**.**

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 April 1998 to June 2003, and was finalised in the meeting of the Standing Committee on the Food Chain and Animal Health on 4 July 2003.

[1] OJ No L 130, 31.05.1996, p.20.

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

The Scientific Committee for Plants was consulted twice, mainly to assess the potential leaching of two metabolites of the active substance, 3-trifluoromethylbenzoic acid (TFMBA) and trifluoroacetic acid (TFAA). In a first opinion[2], the Scientific Committee recommended with respect to TFMBA the inclusion of soils with pH values between 7 and 8 in the sorption studies with this metabolite. As regards the metabolite TFAA, the Committee found the available data insufficient to assess the risk of contamination of ground water. Subsequently, further studies were undertaken by the applicant for both metabolites. In its second opinion[3] the Scientific Committee concluded that concentrations of TFMBA leaching to groundwater from soils with pH above 5 may exceed 0.1 µg/l in a small percentage of cases/situations. The Committee further concluded that the metabolite TFAA does not represent an unacceptable risk to aquatic organisms via groundwater but the toxicological information made available to the Committee was still insufficient. Additional information was subsequently provided and evaluated in the workgroups of the Standing Committee for the Food Chain and Animal Health.

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**[4] concerning the inclusion of flurtamone in Annex I to Directive 91/414/EEC, and to assist the Member States in decisions on individual plant protection products containing flurtamone 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.

---

[2] Opinion of the scientific Committee on Plants regarding the inclusion of flurtamone in Annex I to Council Directive 91/414/EEC concerning the placing of plant protection products on the market

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

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.

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 flurtamone 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 flurtamone containing plant protection product for which Member States will grant or review the authorisation.

Furthermore, these conclusions were reached within the framework of the uses which were proposed and supported by the main data submitter and mentioned in the list of uses supported by available data (attached as Appendix IV to this Review Report).

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 flurtamone 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 0.36% of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet (August 1994). This low intake value reflects the current limited use pattern for this active substance.

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 flurtamone are given in Appendix I.

The active substance shall have a minimum purity of 960 g/kg technical product (based on a pilot 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 flurtamone

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 groundwater, when the active substance is applied in regions with vulnerable soil and/or climate conditions;
- should pay particular attention to the protection of algae and other aquatic plants.

Risk mitigation measures should 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 flurtamone 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 information or monitoring studies to ensure adequate protection of groundwater resources;
- Additional data on dermal absorption.

9. Updating of this review report

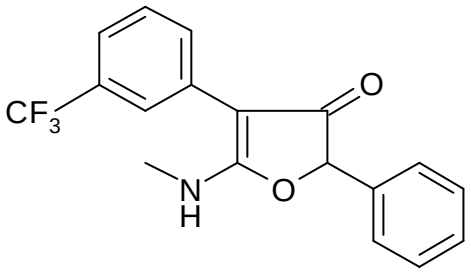
The technical information in this report may require periodic updating to take account of technical and scientific developments as well as of the results of the examination of any information referred to the Commission in the framework of Articles 7, 10 or 11 of Directive 91/414/EEC. Such adaptations 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 flurtamone in Annex I of the Directive.

APPENDIX I

Identity, physical and chemical properties

FLURTAMONE

Common name (ISO)	FLURTAMONE
Development Code (for new actives only)	RE-40885 SX 1802 RPA 590515
Chemical name (IUPAC)	(RS)-5-methylamino-2-phenyl-4-(a,a,a-trifluoro-m-tolyl) furan-3 (2H)-one
Chemical name (CA)	5-[methylamino]-2-phenyl-4-[3-(trifluoromethyl)phenyl]-3(2H)-furanone
CIPAC No	not yet allocated
CAS No	96525 - 23 - 4
EEC No	not yet allocated
FAO SPECIFICATION	not specified
Minimum purity	960 g/kg
Molecular formula	$C_{18}H_{14}F_3NO_2$
Molecular mass	333.3
Structural formula	



Melting point	148.5 ± 1 °C (98.9 and 99.99 % purity)
Boiling point	-
Appearance	light yellow powder
Relative density	1.375 (98.9 and 99.99 % purity)
Vapour pressure	4.5 10^{-9} hPa (20°C - 98.9 purity) 1.8 10^{-8}hPa (30°C – 98.9 % purity)
Henry's law constant	1.3 x 10^{-5} Pa m^3 mol^{-1}
Solubility in water	pH 5 and 20 °C: 10.7 mg/l (99.3 and 99.4 % purity) pH 9 and 20 °C: 10.5 mg/l (99.3 and 99.4 % purity)
Solubility in organic solvents	acetone: 350 g/l acetonitrile: 144 g/l ethyl acetate: 133 g/l DCM: 358 g/l methanol: 199 g/l octanol-1: 25 g/l propanol-2: 44 g/l hexane: 0.018 g/l toluene: 5 g/l
Partition co-efficient (log P_{ow})	2.8 at 40 °C 3.2 at 21 °C
Hydrolytic stability (DT_{50})	pH 5: 11.6 y pH 7: 36.5 y pH 9: 10.5 y
Dissociation constant	not relevant
Quantum yield of direct photo-transformation in water at e >290 nm	3.2 x 10^{-2}
Flammability	non-flammable
Explosive properties	non-explosive
UV/VIS absorption (max.)	neutral pH: 276.2 nm acid pH: 272.6 nm basic pH: 215.6 and 272.6 nm
Photostability in water (DT_{50})	13.1 - 16.8 h

APPENDIX II

END POINTS AND RELATED INFORMATION

FLURTAMONE

1 Toxicology and metabolism

Absorption, distribution, excretion and metabolism in mammals

Rate and extent of absorption:	38 to 43 %, based on the urinary excretion (7 d)
Distribution:	Widely, higher levels in the liver
Potential for accumulation:	Low
Rate and extent of excretion:	Average: Faeces 49 - 61 % - Urine 38 - 43 % (7 d), mostly occuring within 24 h
Toxicologically significant compounds:	Parent compound and its metabolites
Metabolism in animals:	Extensively metabolized using flurtamone labelled on the trifluoromethyl-phenyl ring, aromatic ring hydroxylation, N-demethylation, O-alkylation of the ring-hydroxylated products, hydrolysis of the furan ring and conjugation.

Acute toxicity

Rat LD_{50} oral:	> 5000 mg/kg bw
Rat LD_{50} dermal:	> 2000 mg/kg bw
Rat LC_{50} inhalation:	> 2.2 mg/l
Skin irritation:	Non irritant
Eye irritation:	Non irritant
Skin sensitization (test method used and result):	Not a sensitizer (M&K)

Short term toxicity

Target / critical effect:	Liver: Hepatomegaly, centrilobular hypertrophy
Lowest relevant oral NOAEL / NOEL:	5 mg/kg bw (1 year dog study)
Lowest relevant dermal NOAEL / NOEL:	1000 mg/kg bw (21 day study in rat)

Lowest relevant inhalation NOAEL / NOEL:	Not required

Genotoxicity

	Negative *in vitro* and *in vivo*

Long term toxicity and carcinogenicity

Target / critical effect:	Liver: hypertrophy, centrilobular hypertrophy Kidney: increased amyloidosis in mice
Lowest relevant NOAEL:	2.8 mg/kg bw (2 year rat study)
Carcinogenicity:	No carcinogenic potential

Reproductive toxicity

Target / critical effect - Reproduction:	Reproductive toxic at parental toxic doses
Lowest relevant reproductive NOAEL / NOEL:	25 mg/kg bw (2-generation rat study)
Target / critical effect - Developmental toxicity:	Foetotoxic at maternal toxic doses
Lowest relevant developmental NOAEL / NOEL:	20 mg/kg bw (rabbit)
Delayed neurotoxicity	No indication of neurotoxicity in standard short term and long term studies
Other toxicological studies	Based on available data, no further study required
Medical data	Currently limited as flurtamone is a new active substance

Summary

	Value	Study	Safety factor
ADI:	0.03 mg/kg bw	2-year rat study	100
AOEL systemic:	0.02 mg/kg bw	1-year dog study (adjusted for oral absorption)	100
ARfD (acute reference dose):	Not allocated in view of the toxicological profile of the substance.		

Dermal absorption

	38 % default value (see oral absorption value)

2 Fate and behaviour in the environment

2.1 Fate and behaviour in soil

Route of degradation

Aerobic:

Mineralization after 100 days:	24 - 40 % (366 d)
Non-extractable residues after 100 days:	32 % (366 d)
Major metabolites above 10 % of applied active substance: name and/or code % of applied rate (range and maximum)	RE 54488 (TFMBA) : 8.3 % - 10.8 % TFAA : 9.8 %

Supplemental studies

Anaerobic:	no data
Soil photolysis:	not relevant
Remarks:	none

Rate of degradation

Laboratory studies

DT_{50}lab (20 °C, aerobic):	Flurtamone : 48 - 211 d TFMBA : 11.2 – 16.7 d TFAA : 2 years Normalized DT_{50} used for Focus simulation Flurtamone : 42.8 – 47.6 d (mean : 45.2) TFMBA : 7.3-10.5 (mean 8.9d) TFAA : 2 years
DT_{90}lab (20 °C, aerobic):	Flurtamone : 170 - > 300 d
DT_{50}lab (10 °C, aerobic):	no data
DT_{50}lab (20 °C, anaerobic):	no data

Field studies (country or region)

DT_{50f} from soil dissipation studies:	Flurtamone : 46 - 65 d
DT_{90f} from soil dissipation studies:	Flurtamone : 152 - 216 d
Soil accumulation studies:	not relevant
Soil residue studies:	No data : not required

Remarks: e.g. effect of soil pH on degradation rate	none

Adsorption/desorption

K_f / K_{oc}: K_d:	Flurtamone : K_{oc} 88 – 543 (mean = 329) TFMBA : K_f = 0.36-1.94 ; K_{oc} = 15-52 (mean = 32.5) ; 1/n = 0.52-0.81 TFAA : K_d = 0.3-11 ; K_{oc} = 3.2-27.5 (mean = 22.9) for soils with low pH
pH dependence:	no pH dependency for flurtamone within the range of the studied soils; for TFMBA pH dependency

Mobility

Laboratory studies:

Column leaching:	3 - 50 %
Aged residue leaching:	6.2 % of ^{14}C - RE54488 < 2.93 %

Field studies:

Lysimeter/Field leaching studies:	325 g/ha 0.4 - 3.7 µg/l TFAA 0.03 - 0.11 µg/l TFMBA < 0.01 µg/l Flurtamone

Remarks:	none

2.2 Fate and behaviour in water

Abiotic degradation

Hydrolytic degradation:	pH 5.0 (25 °C) : stable pH 7.0: stable pH 9.0: stable
Major metabolites:	none
Photolytic degradation:	Artificial sunlight : 23 h; pH = 5, 25 °C Flurtamone (final conc) 28.3 % RPA 203597: 33.5 %
Major metabolites:	See above

Biological degradation

Readily biodegradable:	no data
Water/sediment study:	
DT_{50} water:	22 - 24 d
DT_{90} water:	74-79 d
DT_{50} whole system:	59 - > 100 d
DT_{90} whole system:	> 100 d
Distribution in water / sediment systems (active substance)	Sed 22 - 57 % extracted, 18 – 28 % unextracted at 99 d
Distribution in water / sediment systems (metabolites)	less than 10 %
Accumulation in water and/or sediment:	Not expected in water, not significant in sediment

Degradation in the saturated zor

	not relevant

Remarks:

	none

2.3 Fate and behaviour in air

Volatility

Vapour pressure:	1.8 10^{-8}hPa (30°C) - 4.5 10^{-9} hPa (20°C)
Henry's law constant:	1.3 x 10^{-5} Pa m^3 mol^{-1}

Photolytic degradation

Direct photolysis in air:	no data
Photochemical oxidative degradation in air	DT_{50} = 2 h
DT_{50}:	
Volatilisation:	from plant surfaces: not relevant from soil: not relevant

Remarks:	none

3 Ecotoxicology

Representative preparations:

EXP30930	250 g/L flurtamone + 100 g/L diflufenican
EXP30985	94 g/L flurtamone + 350 g/L aclonifen

Terrestrial Vertebrates

Acute toxicity to mammals:	LD_{50} (rat) > 5 000 mg/kg NOAEL = 1 000 ppm food
Acute toxicity to birds:	LD_{50} (bobwhite quail) > 2 530 mg/kg
Dietary toxicity to birds:	LC_{50} (bobwhite quail) > 6 000 ppm LC_{50} (mallard duck) = 2 000 ppm
Reproductive toxicity to birds:	NOEC (bobwhite quail) = 80 ppm NOEC (mallard duck) = 200 ppm
Long term oral toxicity to mammals:	NOEL / NOAEL = 20 mg/kg b.w. (rabbit)

Aquatic Organisms

Acute toxicity fish:	a.s.: LC_{50}: 7.0 mg/l (96 h, *O. mykiss*) EXP30930:LC_{50}: 56 mg/l (96 h, *O. mykiss*) EXP30985:LC_{50}: 1.8 mg/l (96 h, *O. mykiss*) Trifluoroacetic acid: EC_{50} > 1 200 mg/l (96 h, *B. rerio*)
Long term toxicity fish:	a.s.: LC_{50}: 0.63 mg/l (28 d, *O. mykiss*)
Bioaccumulation fish:	BCF = 27 - 28 (whole)
Acute toxicity invertebrate:	a.s.: EC_{50}: 13.0 mg/l (48 h, *D. magna*) EXP30930:EC_{50}: 28 mg/l (48 h, *D. magna*) Trifluoroacetic acid: EC_{50}> 1 200 mg/l (48 h, *D. magna*)
Chronic toxicity invertebrate:	a.s.: NOEC: 0.071 mg/l (21 d, *D. magna*)
Acute toxicity algae:	a.s.: EC_{50b}: 0.020 mg/l (72 h, *S. capricornutum*) EXP30930: EC_{50b}: 0.018 mg/l (72 h, *S. subspicatus*) EXP30985: EC_{50b}: 0.009 mg/l (72 h, *S. capricornutum*) Trifluoroacetic acid: EC_{50b}:

	4.8 mg/l (72 h, *S. capricornutum*)
Chronic toxicity sediment dwelling organism:	a.s.: NOEC: 0.1 mg/l (22 d, *C. riparius*)
Toxicity aquatic plants:	a. s.: EC_{50}: 0.0099 mg/l (14 d, *L. gibba*)

Honeybees

Acute oral toxicity:	LD_{50} > 304 µg flurtamone/bee LD_{50} (EXP30930) > 200 µg flurtamone/bee
Acute contact toxicity:	LD_{50} > 100 µg flurtamone/bee LD_{50} (EXP30985) > 500 µg flurtamone/bee

Other arthropod species

Test species	% Effect
Aphidius rhopalosiphi (adult)	66.2 % survival; parasitation capacity (250 g/ha EXP30930)
Typhlodromus pyri	8.9 % survival; egg production (250 g/ha EXP30930)
Pardosa sp. (adult)	4 % survival; predatory capacity (250 g/ha EXP30930)
Poecilus cupreus (adult)	31 % mortality; feeding rates (250 g/ha EXP30930)
Pardosa sp. (adult)	13.5 % resp. 18.0 % survival; predatory capacity (376 g/ha EXP30985)
Poecilus cupreus (adult)	14 % mortality; feeding rates (376 g/ha EXP30985)

Earthworms

Acute toxicity:	LC_{50} > 1 800 mg as/kg dry soil LC_{50} > 1 000 mg EXP30930/kg dry soil LC_{50} > 1 000 mg EXP30985/kg dry soil
Reproductive toxicity:	not required

Soil micro-organisms

Nitrogen mineralization:	no significant decrease (< 25 %)
Carbon mineralization:	flurtamone: a slight stimulation of soil respiration (less than 15 %) EXP30930: no effect

APPENDIX III

FLURTAMONE

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

B.6 Toxicology and metabolism

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not
IIA 5.1.	Totis, M.	2000	Rat Supplemental A.D.M.E. and Blood Kinetics Study. Aventis CropScience, Sophia-Antipolis Study SA98335, GLP 268 pages Document C031454 unpublished property of Bayer CropScience

B.7 Residue data

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not
IIA 2.6.2	Semino, G	1999	**Trifluoroacetic acid: Health Effect Risk Assessment.** Rhone-Poulenc Agro, Sophia-Antipolis 11 pages Document C019618 unpublished property of Bayer CropScience

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not
IIA 2.6.2	Airaksinen, M. M. and Tammisto, T	1968	Toxic actions of the metabolites of halothane : LD_{50} and some metabolic effects of trifluorethanol and trifluoracetic acid in mice and guinea pigs, *Ann. Med. Exp. Biol. Finniae*, **46** : 242-248
IIA 2.6.2	Blake, D.A., Barry J.G. and Cascorbi H.F.	1970	Effect of trifluoroacetate on the growth of rat liver Naunyn-Schmiedesbergs Arch. Pharmakol 265(5): 474-475
IIA 2.6.2	Blake D.A., Diblasi M.C. and Gorgon G.B.	1981	Absence of mutagenic activity of trifluoroethanol and its metabolites in *Salmonella typhimurium* Fundam Appl Toxicol. 1(6):415-8.
IIA 2.6.2	ECETOC working group	1995	1,1,1,2-Tetrafluoroethane (HFC-134a) JACC No 31 February
IIA 2.6.2	ECETOC working group	1996	1,1-Dichloro-2,2,2--Trifluoroethane (HFC-134a) JACC No 33 February
IIA 2.6.2	Ford D.J., Coyle D.E., and Harrington J.F.	1984	Effects of hypersensitivity to a haolthane metabolite on haltothane-induced liver damage Anaesthesiol. 60(2): 141-143
IIA 2.6.2	Fraser, J.M. and Kaminsky L.S	1988	2,2,2-trifluoroethanol Intestinal and Bone marrow Toxicity: the role of its metabolism to 2,2,2-Trifluoroacetaldehyde and Trifluoroacetic acid Toxicology and applied Pharmacology. 94, 84-92
IIA 2.6.2	Ghantous H., Parnerud I. Danielsson B.R.G. and Dencker L	1986	Distribution of halothane and the metabolites trifluoroacetic acid and bromide in the conceptus after halothane inhalation by pregnant mice. Acta Pharmacol. Toxicol. 59: 370-376
IIA 2.6.2	Just W.W., Gorgas F.U., Heinemann P., Salzer M. and Schimassek	1989	Biochemical effect of zonal heterogenicity of peroxisome proliferation induced by perfluorocarboxylic acids in rat liver. hepatology (Baltimore) 9(4): 570-581
IIA 2.6.2	Kheilo, L.S. and Kremneva S.N.	1966	Comparative assessment of the toxicity of trifluoroacetic acid and pentafluoropropionic acids. Gigiena truda i prof. Zabol. 10(3): 13-17

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not
IIA 2.6.2	Lloyd S.C., Blackburn D.M. and Forster P.M.D.	1988	,Trifluoroethanol and it oxidative metabolites: comparison of in vivo and in vitro effects of rat testis. Toxicol. and Applied Pharmacol. 92, 390-401.
IIA 2.6.2	Longstaff E., Robinson, M, Bradbrook C., Styles J.A. and Purchase I.F.H.	1984	Genotoxicity and carcinogenicity of fluorocarbons: assessment bu short-term in vitro tests and chronic exposure in rats Toxicol Appl Pharmacol. 72(1):15-31.
IIA 2.6.2	Mathieu A., Padua D., Mills J. and Kahan B	1974	Experimental immunity to a metabolite of halothane and fluroxene. Anaesthesiol. 40(4): 385-390
IIA 2.6.2	Patty, F.A.	1963	Industrial Hygiene and Toxicology, vol II, 2nd revised edit., pp. 1801-1803
IIA 2.6.2	Reves J.G and McCracken L.E.	1976	Failure to induce hepatic pathology in animals sensitized to a halothane metabolite and subsequently challenged with halothane. Anest Analg. 55(2): 235-274.
IIA 2.6.2	Stier A., Kunz H.W., Walli A.K. and Schimassek H.	1972	Effects on growth and metabolism of rat liver by halothane and its metabolite trifluoroacetate Biochem. Pharmacol. 21: 2181-2192
IIA 2.6.2	Warheit D.B.	1993	Mechanistic studies with HCFC-123. Du Pont company unpublished data, Haskell laboratory Report HLR 828-92
IIA 2.6.2	Waskell, L.A	1978	. A study of the mutagenicity of anesthetics and their metabolites, *Mut. Res.*, **57** : 141-153.
IIA 6.1	Oliver R.G., Potts K.	2000	(14C)-Flurtamone: Metabolism in wheat. Aventis CropScience, Ongar Study 14704, GLP 181 pages Document C018873 unpublished property of Bayer CropScience

B.8 Environmental fate and behaviour

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not
IIA 7.1.1.2.1	Burr C.M.	1999	(14C)-3-trifluoromethylbenzoic acid rate of degradation in three soils. Rhone-Poulenc Agriculture Ltd Study 15616, GLP 152 pages Document C019620 unpublished property of Bayer CropScience
IIA 7.1.2	Simmonds M.B., Burr C.M.	1999	(14C)-3-trifluoromethylbenzoic acid adsorption/desorption to and from four soils. Rhone-Poulenc Agriculture Ltd, Ongar Study 15618, GLP 121 pages Document C019621 unpublished property of Bayer CropScience
IIA 7.1.1.1.2 & IIA 7.1.1.2	Simmonds M.B., Burr C.M.	1999	(14C)-flurtamone anaerobic soil degradation. Rhone-Poulenc Agriculture Ltd, Ongar Study GD15617, GLP 98 pages Document R011444 unpublished property of Bayer CropScience
IIIA 7.1.1.2 & IIIA 9.1.3 & IIIA 9.2.1	Hardy I.A.J.	1999	Flurtamone: Estimation of DT50 at 10°C, Predicted Environmental Concentrations of TFMBA and TFAA in Groundwater (PECgw) and TFMBA in Soil (PECsoil). Rhone-Poulenc Agriculture Limited, Ongar 9 pages Document C031455 unpublished property of Bayer CropScience

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not
IIIA 9.2.3	Hardy I.A.J.	1999	Flurtamone: Predicted Environmental Concentration in Sediments (PEC_{sed}) Calculation of PEC. Rhone-Poulenc Agriculture Limited, Ongar 8 pages Document C031456 unpublished property of Bayer CropScience
IIIA 9.2.1	Hardy I.A.J.	2002	Predicted Environmental Concentrations in groundwater (PEC_{gw}) of Flurtamone and its metabolites TFMBA and TFAA using the FOCUS groundwater scenarios. Battelle AgriFood Ltd, Ongar Study CX/02/014 61 pages Document C025031 unpublished property of Bayer CropScience

B.9 Ecotoxicology

Annex point/ reference number	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not
IIA 8.6	Turner M.T.F.	1999	The testing of 3-trifluoromethylbenzoic acid (alpha,alpha,alpha,trifluoro-m-toluic acid) for pre- and post-emergence herbicidal acitivity: GLP glasshouse study - UK 1999. Rhone-Poulence Agiculture Ltd, Ongar Study 202136, GLP 33 pages Document C019616 unpublished property of Bayer CropScience

APPENDIX IV

FLURTAMONE

List of uses supported by available data

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		
Winter barley Winter rye	Germany	BACARA EXP30930	F	Broad-leaved weeds and some grasses	SC	250	Spraying	post emergence still tilling	1		0.0625 – 0.125	200/400	0.250	150	
Winter barley Winter rye Winter wheat Tritical	UK	BACARA EXP30930	F	Broad-leaved weeds and some grasses	SC	250	Spraying	pre-emergence post emergence up to Z 32	1		0.0625 – 0.125	200/400	0.125 – 0.25	150	
Winter barley Winter wheat	France	BACARA EXP30930	F	Broad-leaved weeds and some grasses	SC	250	Spraying	post emergence, 3-4 leaf stage Z 13-14	1		0.0625 – 0.125	200/400	0.250	150	
Winter barley Winter wheat	UK	EXP 31165	F	Broad-leaved weeds and some grasses	SC	67	Spraying	post emergence 1-2 leaves to 2nd node and possible pre-emergence	1		0.0625 – 0.125	200/400	0.250	150	

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

(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)

(i) g/kg or g/l

(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on

(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
(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