



EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate E - Food Safety: Production and distribution chain
Unit E.3 - Chemicals, contaminants and pesticides

Beflubutamid

SANCO/T13/07-rev. final

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

Review report for the active substance **beflubutamid**

Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 15 May 2007 in view of the inclusion of beflubutamid 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 beflubutamid, 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 German authorities received on 27 June 2000 an application from a Task Force consisting of UBE Europe GmbH and Stähler Agrochemie GmbH & Co. KG (after UBE Europe GmbH having later left the Task Force, now: Stähler International GmbH & Co. KG)¹, hereafter referred to as the applicant, for the inclusion of the active substance beflubutamid in Annex I to the Directive. The German authorities indicated to the Commission on 21 July 2000 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 beflubutamid was distributed to the Member States and the Commission.

¹ On 03 May 2007 Stähler International GmbH & Co. KG informed the German authorities, that UBE Europe GmbH has transferred all rights regarding the relevant data, dossiers, applications and associated rights to Stähler International GmbH & Co. KG, which therefore is to be considered as the sole applicant.

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 18 October 2000, 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 2000/784/EC² of 4 December 2000 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 Germany, as rapporteur Member State, would carry out the detailed examination of the dossier and report the conclusions of the 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.

Germany submitted to the Commission on 13 August 2002 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 beflubutamid 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 Task Force consisting of UBE Europe GmbH and Stähler Agrochemie GmbH & Co. KG (now Stähler International GmbH & Co. KG) on 3 September 2002.

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 Pesticide Safety Directorate (PSD) in York, United Kingdom, from February to September 2003.

² OJ L 311, 12.12.2000, p. 47.

The report of the peer review (in this case the final reporting table) was circulated, for further consultation, to Member States and the Task Force (UBE Europe GmbH and Stähler Agrochemie GmbH & Co. KG (now Stähler International GmbH & Co. KG)) on 22 October 2003.

The dossier, revised draft assessment report and the peer review 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 all Member States. This final examination took place from September 2004 to December 2006, and was finalised in the meeting of the Standing Committee on 15 May 2007.

The present review report contains the conclusions of this final examination; given the importance of the revised draft assessment report, the peer review report and the comments and clarifications submitted after the revision of the draft assessment report 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 review of beflubutamid did not reveal any open questions or concerns, which would have required a consultation of the Scientific Committee on Plants or of the European Food Safety Authority which has taken over the role of that 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 2007/50/EC³ concerning the inclusion of beflubutamid in Annex I to Directive 91/414/EEC, and to assist the Member States in decisions on individual plant protection products containing beflubutamid 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.

³ OJ L 202, 3.8.2007, p. 15.

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 beflubtamid 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 beflubtamid 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 sole 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 beflubtamid 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 5.2 % of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet (1998). This low intake value reflects the current limited use pattern for this active substance. The acute intake calculation was performed based on the ADI of 0.02 mg/kg bw/day.

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 beflubutamid are given in Appendix I.

The active substance shall have a minimum purity of 970 g/kg technical product.

The review has established that for the active substance notified by the applicant (Task Force UBE Europe GmbH and Stähler Agrochemie GmbH & Co. KG (now Stähler International GmbH & Co. KG)), 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 beflubutamid

On the basis of the proposed and supported uses, the following particular issues have been identified as requiring particular and short term (within 12 months at the latest) attention from the Member States, in the framework of any authorisations to be granted, varied or withdrawn, as appropriate:

Member States must pay particular attention to the risk to aquatic organisms.

Conditions of use shall include risk mitigation measures, 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 beflubutamid in Annex I.

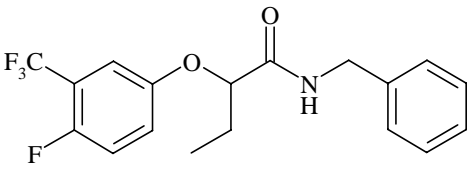
9. Updating of this review report

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 beflubutamid in Annex I of the Directive.

APPENDIX I

Identity, physical and chemical properties

BEFLUBUTAMID

Common name (ISO)	Beflubutamid
Development Code (for new actives only)	UBH-820, UR-50601
Chemical name (IUPAC)	(<i>RS</i>)- <i>N</i> -benzyl-2-(4-fluoro-3-trifluoromethylphenoxy)butanamide
Chemical name (CA)	2-[4-fluoro-3-(trifluoromethyl)phenoxy]- <i>N</i> -(phenylmethyl)butanamide
CIPAC No	662
CAS No	113614-08-7
EEC No	Not available
FAO SPECIFICATION	Not yet published
Minimum purity	970 g/kg (racemetic mixture)
Molecular formula	C ₁₈ H ₁₇ F ₄ NO ₂
Molecular mass	355.12 g/mol
Structural formula	

Melting point	75 °C (99.98 %)
Boiling point	Decomposition
Appearance	White fluffy powder (99.98 % and 97.46 %)
Relative density	1.33 (99.98 %)
Vapour pressure	$1.1 \cdot 10^{-5}$ Pa at 25 °C
Henry's law constant	$1.1 \cdot 10^{-4}$ Pa m ³ mol ⁻¹
Solubility in water	<p>$2.30 \cdot 10^{-3}$ g/L at 10 °C</p> <p>$3.29 \cdot 10^{-3}$ g/L at 20 °C</p> <p>$5.03 \cdot 10^{-3}$ g/L at 30 °C</p> <p>Preliminary work showed that the water solubility did not change significantly with pH.</p>
Solubility in organic solvents	<p>Acetone > 600 g/L at 20 °C</p> <p>1,2-Dichloroethane > 544 g/L at 20 °C</p> <p>Ethylacetate > 571 g/L at 20 °C</p> <p>Methanol > 473 g/L at 20 °C</p> <p><i>n</i>-Heptane = 2.18 g/L at 20 °C</p> <p>Xylene = 106 g/L at 20 °C</p>
Partition co-efficient (log P_{ow})	<p>No pH dependency.</p> <p>log P_{OW} = 4.28 at 21 °C</p>
Hydrolytic stability (DT₅₀)	pH : 5 no degradation (50 °C)
	pH : 7 no degradation (50 °C)
	pH : 9 no degradation (50 °C)
Dissociation constant	Dissociation is unlikely
Quantum yield of direct photo-transformation in water at λ >290 nm	0.044 (pH 7)
Flammability	Neither highly flammable nor autoflammable
Explosive properties	Not explosive
UV/VIS absorption (max.)	281.5 nm
Photostability in water (DT₅₀)	DT ₅₀ 48 d (pH 7; 25 °C)

APPENDIX II

END POINTS AND RELATED INFORMATION

BEFLUBUTAMID

1 Toxicology and metabolism

Absorption, distribution, excretion and metabolism in mammals

Rate and extent of absorption:	At 35 mg/kg bw rapidly and nearly completely absorbed (>80 %) based on excretion via bile (>66 %) and urine (8 – 16 %). Plasma C _{max} : 6 hours
Distribution:	Widely distributed highest levels found in kidneys and liver.
Potential for accumulation:	No evidence for accumulation
Rate and extent of excretion:	Completely excreted within 120 hours mainly via bile (At 35 mg/kg – 66 % (females) and 85 % (males)). Urinary excretion was found to be higher in females.
Toxicologically significant compounds:	Parent compound and major metabolites
Metabolism in animals:	Extensively metabolised by hydroxylation, cleavage of the amide bond and conjugation as glucuronides (major metabolites: phenoxybutyric acid, hippuric acid)

Acute toxicity

Rat LD ₅₀ oral:	>5000 mg/kg bw
Rat LD ₅₀ dermal:	>2000 mg/kg bw
Rat LC ₅₀ inhalation:	>5 mg/L air/4h (nose only)
Skin irritation:	Non-irritant
Eye irritation:	Non-irritant
Skin sensitization (test method used and result):	Non-sensitising (M & K)

Short term toxicity

Target / critical effect:	Decreased bw; liver (rat,mouse,dog), kidney + thyroid gland (rat)
Lowest relevant oral NOAEL / NOEL:	90-d oral, rat: 400 ppm (30 mg/kg bw/d)
Lowest relevant dermal NOAEL / NOEL:	No data - Not required

Lowest relevant inhalation NOAEL / NOEL:

No data - Not required

Genotoxicity

No evidence of genotoxic potential. Based on the levels in blood/plasma there was sufficient evidence that the bone marrow would be exposed in the in vivo assay.

Long term toxicity and carcinogenicity

Target / critical effect:

Liver, kidney + thyroid gland (rat)

Lowest relevant NOAEL:

104-wk oral, rat: 50 ppm (2.2 mg/kg bw/d)

Carcinogenicity:

Not carcinogenic in mice. Equivocal increase in thyroid follicular cell tumours in male rats at highest dose (3200 ppm) in the 2 year study. No convincing information on the mechanism of possible tumour induction; relevance to man, if any, considered low because of the high margin of safety between ADI and NOEL for neoplasia.

Reproductive toxicity

Target / critical effect - Reproduction:

There were no specific effects on reproduction. Impairment of bodyweight development during lactation, delay in age for vaginal opening (F1-females) at parental toxic doses; offspring kidney changes at 3200 ppm.

Lowest relevant reproductive NOAEL / NOEL:

2-gen. rat:
Reproductive Outcome: 3200 ppm (320 mg/kg bw/day)
Parental toxicity; 200 ppm (approx. 17 mg/kg bw/day)
Pup development; 200 ppm (approx. 17 mg/kg bw/day)

Target / critical effect - Developmental toxicity:

Developmental effects on the kidney/ureter (vestigial and/or losses of renal papilla, dilatated ureter) at maternally toxic doses.

Lowest relevant developmental NOAEL / NOEL:

100 mg/kg bw/d (rat, rabbit)

Delayed neurotoxicity

No concern of neurotoxic effects from toxicity studies; no data for delayed neurotoxicity - not considered necessary

Other toxicological studies

No data, not required.

Medical data

Limited data (new compound);
no human health problems reported

Summary

	Value	Study	Safety factor
ADI:	0.02 mg/kg bw	104-wk, oral rat	100
AOEL systemic:	0.3 mg/kg bw/d	90-d, rat	100
AOEL inhalation:	Not required	-	-
AOEL dermal:	Not required	-	-
ARfD (acute reference dose):	Not necessary. Not allocated.	-	-

Dermal absorption

No studies performed; 100 % assumed (worst case)

2 Fate and behaviour in the environment

2.1 Fate and behaviour in soil

Route of degradation

Aerobic:

Mineralization after 100 days:

12.2 - 46.8 % (phenoxy label; 120 or 152 d)
 55.1 % (benzylamine label; 152 d)

Non-extractable residues after 100 days:

31.8 - 50.5 % (phenoxy label; 120 or 152 d)
 25.8 % (benzylamine label; 152 d)

Major metabolites above 10 % of applied active substance: name and/or code % of applied rate (range and maximum)

Phenoxybutyric acid / UR-50604:
 9.0 – 26.1 % (phenoxy label)

Supplemental studies

Anaerobic:

CO₂: not detected (both labels)

Non-extractable residues:

4.1 % (phenoxy label; 120 d);

19.4 % (benzylamine label; 120 d)

Major metabolite:

Phenoxybutyric acid / UR-50604:

23.1 % (phenoxy label)

Soil photolysis:

Active substance:

73.1 – 77.9 % after 10 d irradiation

91.8 – 112 % after 10 d (dark control)

Remarks:

None.

Rate of degradation

Laboratory studies

DT_{50lab} (20 °C, aerobic):

Active substance:

DT_{50lab} (20 °C, aerobic, 40 % MWHC) (r²= 0.99)

- Arrow (sandy loam) 15.8 d

- Wick (sandy loam) 5.3 d

- Speyer 2.2 (loamy sand) 98.7 d

- Speyer 2.2 (loamy sand) 20.6 d

- Evesham 3 (sandy clay loam) 8.7 d

	<p>Metabolite UR-50604:</p> <p>DT_{50lab} (20 °C, aerobic, 40 % MWHC) ($r^2=0.99$)</p> <p>Arrow (sandy loam) 18 d</p> <p>- Wick (sandy loam) 0.9 d</p> <p>- Speyer 2.2 (loamy sand) 7.7 d</p> <p>- Speyer 2.2 (loamy sand) 3.1 d</p> <p>- Evesham 3 (sandy clay loam) 3.6 d</p>
DT _{90lab} (20 °C, aerobic):	<p><u>Active substance:</u></p> <p>DT_{90lab} (20 °C, aerobic) ($r^2=0.99$)</p> <p>- Arrow 52.5 d</p> <p>- Wick 17.4 d</p> <p>- Speyer 2.2^A 328.0 d</p> <p>- Speyer 2.2^B 68.4 d</p> <p>- Evesham 3 29.1 d</p>
	<p><u>Metabolite UR-50604:</u></p> <p>DT_{90lab} (20 °C, aerobic) ($r^2=0.99$)</p> <p>- Arrow 59.8 d</p> <p>- Wick 3.2 d</p> <p>- Speyer 2.2^A 25.6 d</p> <p>- Speyer 2.2^B 12.0 d</p> <p>- Evesham 3 10.3 d</p>
DT _{50lab} (10 °C, aerobic):	<p><u>Active substance:</u></p> <p>DT_{50lab} (10 °C, aerobic) ($r^2=0.99$)</p> <p>- Evesham 3 20 d</p>
	<p><u>Metabolite UR-50604:</u></p> <p>DT_{50lab} (10 °C, aerobic) ($r^2=0.99$)</p> <p>- Evesham 3 80 d</p>
DT _{50lab} (20 °C, anaerobic):	<p><u>Active substance:</u></p> <p>DT_{50lab} (20 °C, anaerobic):</p> <p>- water phase 4 d ($r^2=0.99$)</p> <p>- soil 260 d ($r^2=0.96$)</p>
	<p>DT_{90lab} (20 °C, anaerobic):</p> <p>- water phase 12 d ($r^2=0.99$)</p>
	degradation in the saturated zone: no data

Field studies (country or region)DT_{50f} from soil dissipation studies:DT_{50f}:Active substance:

Autumn use:

Spain 103 d (r²=0.97)United Kingdom 51 d (r²=0.99)

Spring use:

Spain 86 d(r²=0.97)

Summer use:

Germany North 20 d (r²=0.86)Germany South 15 d (r²=0.79)Metabolite UR-50604:

< 10 –16 µg/kg between 59 – 126 d

DT_{90f} from soil dissipation studies:DT_{90f}:Active substance:

Autumn use:

Spain 343 d

United Kingdom 169 d

Spring use:

Spain 285 d

Summer use:

Germany North 65 d

Germany South 49 d

Soil accumulation studies:

No accumulation.

Soil residue studies:

Laboratory studies (results expressed as mg
equivalents active substance / kg soil dry weight):Active substance:carrot 0.083 mg/kg (30 d); wheat 0.056 mg/kg
(30d), 0.005 mg/kg (193 d).Metabolite UR-50604:

carrot 0.024 mg/kg (30 d); wheat 0.019 (30 d).

Remarks:

e.g. effect of soil pH on degradation rate

None.

Adsorption/desorption

K_f / K_{oc} :

Active substance:				
Soil	pH	K_f	K_{oc}	1/n

Arrow	6.4	26.7	1335	0.93
Wick	5.8	8.5	1061	0.92
Speyer 2.2	6.0	43.0	1793	0.92
Evesham 3	7.1	16.2	496	0.86
Metabolite UR-50604				
Wick	5.8	0.2	22	0.93
Speyer 2.2	6.0	0.2	9	0.81
Evesham 3	7.1	0.1	6	0.57
Not calculated.				
No				

K_d :

pH dependence:

Mobility

Laboratory studies:

Column leaching:

Not tested; mobility assessed in adsorption/desorption studies

Aged residue leaching:

Not tested; mobility assessed in adsorption/desorption studies

Field studies:

Lysimeter/Field leaching studies:

Lysimeter or field leaching studies not performed.

Remarks:

None.

2.3 Fate and behaviour in air

Volatility

Vapour pressure:

$1.1 \cdot 10^{-5}$ Pa at 25 °C

Henry's law constant:

$1.1 \cdot 10^{-4}$ Pa m³ mol⁻¹

Photolytic degradation

Direct photolysis in air:

Model: Aqueous solution

Active substance:

DT₅₀ 48 d (first order kinetics) at pH 7 (25 °C)

Metabolite UR-50604:

DT₅₀ 21 (pH 5), 24 (pH 7) and 20 d (pH 9)

Photochemical oxidative degradation in air

DT₅₀:

DT₅₀ = 3.5 hours (12 h day) and 15.7 hours (24h day), respectively (according to Atkinson calculation)

Volatilisation:

from plant surfaces: no data

from soil: no data

Remarks:

None.

3 Ecotoxicology

Terrestrial Vertebrates

Acute toxicity to mammals:	LD ₅₀ > 5000 mg/kg (rat)
Acute toxicity to birds:	LD ₅₀ > 2000 mg/kg (bobwhite quail)
Dietary toxicity to birds:	LC ₅₀ > 5200 ppm (> 970 mg/kg bw/d, bobwhite quail)
Reproductive toxicity to birds:	NOEL 1000 ppm (88 mg/kg bw/d, bobwhite quail)
Short-term oral toxicity to mammals:	NOAEL 400 ppm (30 mg/kg bw/d, 90-d oral, rat)
Long-term toxicity to mammals:	NOAEL 200 ppm (17 mg/kg bw/d, for reproductive effects in rat multi-generation study)

Aquatic Organisms

	Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L) *
Laboratory tests					
Acute toxicity fish:	<i>O. mykiss</i>	Active substance	acute	Mortality EC ₅₀	1.86
	<i>O. mykiss</i>	Metabolite UR-50604	acute	Mortality EC ₅₀	>93
	<i>O. mykiss</i>	ASU 95 510 H	acute	Mortality EC ₅₀	39.1
Long term toxicity fish:	<i>P. promelas</i>	Active substance	long-term	Growth NOEC	0.11
Bioaccumulation fish:	<i>O. mykiss</i>	Active substance	---	---	BCF 140 (whole fish)
Acute toxicity invertebrate:	<i>D. magna</i>	Active substance	acute	Immobilization EC ₅₀	1.64
	<i>D. magna</i>	Metabolite UR-50604	acute	Immobilization EC ₅₀	>91
	<i>D. magna</i>	ASU 95 510 H	acute	Immobilization EC ₅₀	17.3
Chronic toxicity invertebrate:	<i>D. magna</i>	Active substance	chronic	Reproduction NOEC	0.455
Acute toxicity algae:	<i>S. capricornutum</i>	Active substance	chronic	Biomass EC ₅₀	0.00455
	<i>A. flos-aquae</i>	Active substance	chronic	Biomass EC ₅₀	> 3.31
Chronic toxicity sediment dwelling organism:	<i>C. riparius</i>	Active substance	long-term	Emergence NOEC	1.8

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L) *	
Long-term toxicity aquatic plants: Microcosm or mesocosm tests: None.	<i>C. riparius</i>	Active substance	chronic	Emergence NOEC	0.56
	<i>L. gibba</i>	Active substance	long-term	Fronds	0.02

*: with exception of the *C. riparius* test (nominal concentration) all concentrations were given as measured, maximum water solubility of beflubutamid is 3.31 mg/L

Honeybees

Acute oral toxicity:

LD ₅₀ > 200 µg/bee

Acute contact toxicity:

LD ₅₀ > 200 µg/bee

Other arthropod species

Test species	Stage	Test Substance	Dose g as/ha	Endpoint	% Effect
<i>T. pyri</i>	Protonymphs	ASU 92530 H	250	Mortality	8
				Fecundity	9
<i>T. pyri</i>	Protonymphs	ASU 95 510 H	255	Mortality	31
				Fecundity	0
<i>A. rhopalosiphi</i>	Adults	ASU 92530 H	250	Mortality	0
				Fecundity	44
<i>A. rhopalosiphi</i>	Adults	ASU 95 510 H	255	Mortality	3
				Fecundity	13
<i>C. carnea</i>	Larvae	ASU 92530 H	250	Mortality	6
				Fecundity	5
<i>C. carnea</i>	Larvae	ASU 95 510 H	510	Mortality	18
				Fecundity	0
<i>P. cupreus</i>	Adults	ASU 92530 H	250	Mortality	12
				Food uptake	8
<i>P. cupreus</i>	Adults	ASU 95 510 H	510	Mortality	0
				Food uptake	9

Field or semi-field tests

Not required.

Earthworms

Acute toxicity:

Active substance:LC₅₀ 732 mg as/kg
(corrected to 366 mg as/kg)Metabolite UR-50604:LC₅₀ 229 mg/kg

Reproductive toxicity:

NOEC < 0.255 kg as/ha
(form. ASU 92 530 H containing 500 g/L beflubutamid), equivalent to < 0.34 mg as/kg, corrected to < 0.17 mg as/kgNOEC 6 L product/ha
(form. ASU 95 510 H containing isoproturon 500 g/L and 85 g/L beflubutamid), equivalent to 0.68 mg as/kg, corrected to 0.34 mg as/kgMetabolite UR-50604:

NOEC 3.8 mg/kg

Field study:

NOEC 3.0 L/ha
(form. ASU 95 519 H containing isoproturon 500 g/L and 85 g/L beflubutamid), equivalent to 255 g as/ha

Other soil non-target macroorganisms

Reproductive toxicity:

(Collembola / *F. candida*)Preparation Herbaflex

NOEC: 320 mg/kg artificial soil

NOEC_{corr}: 160 mg/kg soil
(due to log P_{OW} = 4.28, i.e > 2)

Soil micro-organisms

Nitrogen mineralization:

Active substance beflubutamid:

Effects < 25 % up to 0.6 kg/ha

Metabolite UR-50604 :

Effects < 25 % up to 0.34 kg/ha

Carbon mineralization:

Active substance beflubutamid:

Effects < 25 % up to 0.6 kg/ha

Metabolite UR-50604 :

Effects < 25 % up to 0.34 kg/ha

APPENDIX III**BEFLUBUTAMID**

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 (where different from company) Company, Report No. GLP or GEP status (where relevant) Published or not
AIIA-1.9; 1.10	Funaki, E.; Okada, T.	2003	Herbicidal activity of Beflubutamid isomers 15.10.2003 UBE not GLP, unpublished CHE2004-162
AIIA-1.10; 1.11	Comb, A.L.	2005	UR-50601: Purity and impurity determination, Huntington Life Science Ltd. UBE Report no. UBE 128/052380, GLP, unpublished CHE2005-980
AIIA-1.11	Anonymous	2003	Document J – Annex II, Amendment No. 3 UBE not GLP, unpublished CHE2004-21
AIIA-4.2.1	Stähler, O.; Frauen, M.; Stähler, R.	2003	Validation of the Analytical Method for the Determination of Beflubutamid (UBH-820) in Cereals (Green Plant, Grain and Straw) according to Method L 00.00-34 "Amtliche Sammlung von Untersuchungsverfahren nach § 35 LMBG " Analytical Method No.: AM-RU-1203, SIT Study-No.: RU0303, Protocol No.: 95510-GM-002D; GLP, unpublished MET2004-86
AIIA-4.2.1	Rogge, K., Siebers, J.	2002	Residue analytical laboratory, BBA (Federal Biological Research Centre) Braunschweig published (www. bvl.bund.de/dbanalytik)
AIIA-4.2.2	Groß, G.	2004	Development of a method for the determination of Fluoromethylphenoxybutyric acid (UR50604) in soil; TSU BioChem project No.: 04 10 35 2002, GLP, unpublished MET2004-288

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
AIIA-4.2.2	Groß, G.	2005	Determination of the residues of the active substance beflubutamid and its metabolite UR50604 in soils from an earthworm field study; TSU BioChem project No.: 0410352012, GLP, unpublished MET2005-776

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
AIIA-5.5, AIIIA-5.3.2	Funaki, E.	2003	Mechanistical explanation for the occurrence of thyroid gland follicular tumours of combined chronic toxicity/carcinogenicity study in rats and their relevance to man (Mode of Action Analysis - UR 50601). UBE Ube Research Laboratory, Ltd., 29.07.2003 not GLP, not published TOX2003-1546

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
AIIA- 7.1.1.1.1; 7.1.1.1.2; 7.1.1.2.1	Funaki, E.	2003	Beflubutamid (UR-50601), Environmental fate issues associated with the isomers of parent UR-50601 and metabolite UR-50604, UBE Industries, UBE 28.11.2003 not GLP, unpublished BOD2004-62
AIIA- 7.1.1.2.1; 7.1.2; AIIIA- 9.1.1.1; 9.1.2.1; 9.1.3	Heimann- Detlefsen, D.	2003	Predicted environmental concentration in soil and water UBE UBE-2003-01, 12.12.2003 not GLP, unpublished BOD2004-63

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
AIIIA-9.1.3	Heimann-Detlefsen, D.	2005	Predicted environmental concentration in soil and water - Amendment 1. UBE UBE-2003-01, Amendment 1, 11.07.2005 not GLP, unpublished BOD2005-954

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
AIIIA-8.4.2	Müther-Paul, J.	2005	Sublethal toxicity of UR-50604 on earthworms, Eisenia fetida using an artificial soil test. UBE 20041457/01-NREf GLP, unpublished ARW2005-258
AIIIA-10.1	Gurney, J.E.; Perrett, J.; Crocker, D.R.; Pasqual, J.A.	1998	Mammal Bible -Mammals and farming: Information for risk assessment. MAFF, CSL Milestone Report AVS2004-28
AIIIA-10.1	Crocker, D.R. et al.	2002	Methods for estimating daily food intake of wild birds and mammals. CSL, Final Report AVS2006-29
AIIIA-10.1	Anonymous	2003	Risk Assessment for Birds. SIT, 2003 not GLP, unpublished AVS2004-43
AIIIA-10.2	Anonymous	2003	Effects on Aquatic organism. SIT, 2003 not GLP, unpublished WAT2004-77
AIIIA-10.3	Anonymous	2003	Risk Assessment for mammals. SIT, 2003 not GLP, unpublished AVS2004-49
AIIIA-10.6	Noack, U.	2003	Herbaflex (Beflubutamid) Assessment of Effects on Earthworm. SIT, 2003 not GLP, unpublished ARW2004-23

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
AIIIA-10.6.1	Heimann-Detlefsen, D.	2005	Effects on Earthworm Population, Risk Assessment with Respect to the Long-Term Effects of Herbaflex (Beflubutamid/Isoproturon), Beflubutamid (UR-50601), and Metabolite (UR-50604). UBE, UBE-2005-01 not GLP, unpublished ARW2005-259
AIIIA-10.6.1.3	Strömel, C.; Teresiak, H.	2005	Field study to evaluate the effects of Herbaflex on earthworms. TSU, AC/STA/04/01 GLP, unpublished ARW2005-260
AIIIA-10.6.1.3	Groß, G.	2005	Determination of the residues of the active substance Beflubutamid and its metabolite UR-50604 in soils from an earthworm field study. TSU, 0410352012 GLP, unpublished ARW2005-261
AIIIA-10.6.2	Bruhnke, C.	2003	Herbaflex - Inhibition of reproduction of collembola (folsomia candida). SIT, 030708SS ICR92952 GLP, unpublished ARW2004-20
AIIIA-10.8	Fiebig, S.	2001	Herbaflex: Terrestrial plants toxicity, seedling emergence, tier II. SIT, TNK77872 GLP, unpublished PFL2001-122
AIIIA-10.8	Fiebig, S.	2001	Herbaflex: Terrestrial plants toxicity, vegetative vigour, tier II. SIT, TNW7787 GLP, unpublished PFL2004-25
AIIIA-10.8	Fiebig, S.	2001	Herbaflex: Standardized bioassay for the determination of ED10 - (NOEL) and ED50 - values for herbicides and selected following crops in soil. SIT, TPB77871 GLP, unpublished PFL2004-26
AIIIA-10.8	Fiebig, S.	2001	ASU92530 H: Standardized bioassay for the determination of ED10 - (NOEL) and ED50 - values for herbicides and selected following crops in soil. SIT, TPB77893 GLP, unpublished PFL2004-27

Codes of company

UBE UBE Industries

SIT Stähler International GmbH & Co. KG

TSU: Task force Stähler International GmbH & Co. KG / UBE Industries

APPENDIX IV

List of uses supported by available data

Beflubutamid

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/ha min max	water l/ha min max	kg as/ha min max		
Winter wheat Winter barley Triticale Winter rye	Northern Europe	ASU 95510H	F	Monocotyledon and dicotyledon weeds Autumn: BBCH 11-13 Spring: BBCH 11-29	SC	85 g/L beflubutamid + 500 g/L isoproturon	spraying	Autumn BBCH 11-29 Spring BBCH 13-29	1	-	<u>Autumn:</u> 0.0425 + 0.250 isoproturon <u>Spring:</u> 0.0425 + 0.250 isoproturon	200-400 200-400	0.085 - 0.170 + 0.500 - 1.000 isoproturon 0.085 - 0.170 + 0.500 - 1.000 isoproturon		Co-formulation with isoproturon

Beflubutamid

APPENDIX IV

List of uses supported by available data

14 February 2007

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/ha min max	water l/ha min max	kg as/ha min max		
Winter wheat Winter barley Durum wheat	Southern Europe	ASU 95510H	F	Monocotyledon and dicotyledon weeds Autumn: BBCH 11-13 Spring: BBCH 11-29	SC	85 g/L beflubutamid + 500 g/L isoproturon	spraying	Autumn BBCH 11-29 Spring BBCH 13-29	1	-	<u>Autumn:</u> 0.0425 + 0.250 isoproturon <u>Spring:</u> 0.0425 + 0.250 isoproturon	200-400 200-400	0.085 - 0.170 + 0.500 - 1.000 isoproturon 0.085 - 0.170 + 0.500 - 1.000 isoproturon		Co-formulation with isoproturon

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)
- (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

- (i) g/kg or g/l
- (j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
- (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