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HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

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

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

Review report for the active substance **flazasulfuron**

Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 28 November 2003 in view of the inclusion of flazasulfuron 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 flazasulfuron, 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 Spanish authorities received on 16 December 1996 an application from ISK Biosciences Europe S.A., hereafter referred to as the applicant, for the inclusion of the active substance flazasulfuron in Annex I to the Directive. Spanish authorities indicated to the Commission on 19 May 1997 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 flazasulfuron 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 29 May 1997, 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 97/865/EC¹ of 5 December 1997 that these requirements were satisfied.

¹ OJ No L351, 23.12.1997, p.67.

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 Spain 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.

Spain submitted to the Commission on 1 August 1999 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 flazasulfuron 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 30 August 1999 as well as to ISK Biosciences Europe S.A. being the sole applicant on 8 September 1999.

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 November 1999 to July 2000.

The report of the peer review (i.e. full report) was circulated, for further consultation, to Member States and the sole applicant on 15 June 2001.

The dossier, draft assessment report and the peer review report (i.e. full report) including in particular an outline resume 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 February 2001 to November 2003, and was finalised in the meeting of the Standing Committee on 28 November 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, these documents are considered respectively as background documents A, B and C to this review report and are part of it.

The review did not reveal any open questions or concerns, which would have required a consultation of the Scientific Committee on Plants.

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 2004/30/EC² concerning the inclusion of flazasulfuron in Annex I to Directive 91/414/EEC, and to assist the Member States in decisions on individual plant protection products containing flazasulfuron 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.

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 flazasulfuron 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 flazasulfuron 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.

² OJ No L 077, 13.03.2004, p. 50.

4. Specific conclusions which are highlighted in this evaluation

4.1 Residues of flazasulfuron 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 0.71 % 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. An acute Reference Dose was not allocated.

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 flazasulfuron are given in Appendix I.

The active substance shall have a minimum purity of 940 g/kg technical product.

The review has established that for the active substance notified by the applicant (ISK Biosciences Europe S.A.), 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 flazasulfuron

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 potential for groundwater contamination, when the active substance is applied in regions with vulnerable soil and/or climatic conditions. Risk mitigation measures should be applied, if appropriate.
- Member States should pay particular attention to the protection of aquatic plants. Risk mitigation measures should be applied, if appropriate.

8. List of studies to be generated

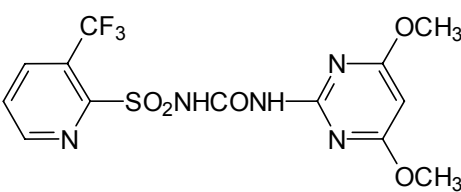
No further studies were identified which were considered at this stage, and under the current inclusion conditions necessary in relation to the inclusion of flazasulfuron in Annex I.

When granting authorisations Member States may require additional information or monitoring studies in critical regions to ensure adequate protection of ground water resources.

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 flazasulfuron in Annex I of the Directive.

APPENDIX I**Identity, physical and chemical properties****FLAZASULFURON**

Common name (ISO)	Flazasulfuron (Proposed to ISO)
Development Code (for new actives only)	SL-160
Chemical name (IUPAC)	1-(4,6-dimethoxypyrimidin-2-yl)-3-(3-trifluoromethyl-2-pyridylsulphonyl)urea
Chemical name (CA)	2-pyridinesulfonamide, N-[[4,6-dimethoxy-2-pyridimidinyl]amino]carbonyl]-3-(trifluoromethyl)
CIPAC No	595
CAS No	104040-78-0
EEC No	Not available
FAO SPECIFICATION	Not available
Minimum purity	940 g/kg
Molecular formula	C ₁₃ H ₁₂ F ₃ N ₅ O ₅ S
Molecular mass	407.36
Structural formula	

Melting point	180 °C. Purity 99.7%
Boiling point	Decomposition initiated at 181.5°C
Appearance	Pure Active Ingredient. Purity 99.7%. Lot # Y920205. White powder. Munsell Color N9.5/90.0%R Technical Grade Active Ingredient. Purity 97.4%. Lot # 303. Granular cream solid. Munsell Color 2.5Y 9/2 Pure Active Ingredient (PAI). Purity 99.7%. Lot # Y920205.Odorless Technical Grade Active Ingredient. Purity 97.4%. Lot # 303. Strong lawn fertilizer.
Relative density	$D_{4}^{20} = 1.623$ Technical Grade Active Ingredient. (99.4%)
Vapour pressure	Vapor pressure at 25°C, 35°C and 45°C was determined to be $< 1.33 \times 10^{-5}$ Pa. Purity 99.8%.
Henry's law constant	2.5799×10^{-6} Pa m ³ mol ⁻¹
Solubility in water	pH <u>5</u> : 0.027 ± 0.003 g/l
	pH <u>7</u> : 2.100 ± 0.05 g/l
	pH <u>9</u> : not stable
Solubility in organic solvents	n-Hexane: 0.5 ± 0.04mg/l
	Toluene: 0.56 ± 0.014g/l
	Dichloromethane: 22.1 ± 0.54g/l
	Methanol: 4.2 ± 0.10g/l
	Acetone: 22.7 ± 0.75g/l
	Ethyl acetate: 6.9 ± 0.21g/l
	n-octanol: 0.20 ± 0.013g/l
	Acetonitrile: 8.7 ± 0.18g/l
Partition co-efficient (log P_{ow})	pH <u>5</u> : logK _{OW} = 1.30
	pH <u>7</u> : log K _{OW} <-0.06
Hydrolytic stability (DT₅₀)	pH <u>4</u> (22 ± 1°C): 17.4 hours
	pH <u>7</u> (22 ± 1°C): 16.6 days
	pH <u>9</u> (22 ± 1°C): 13.1 days
Dissociation constant	pK _a = 4.37 ± 0.08 (20 ± 1 °C)
Quantum yield of direct photo-transformation in water at ε >290 nm	Φ = 1.67 x 10 ⁻²
Flammability	Non-flammable

Explosive properties	Non-explosive
UV/VIS absorption (max.)	$\lambda_{\text{max}} = 241.0$; AU = 0.993; $\epsilon = 17300$ L/mol-cm There are absorptions ($\epsilon > 10$) at $\lambda > 290$ nm.
Photostability in water (DT₅₀)	$t_{1/2} = 8.9$ (P) & 8.0 (Pm) days (sunlight) $t_{1/2} = 17.3$ (P) & 15.9 (Pm) days (dark)

APPENDIX II

END POINTS AND RELATED INFORMATION

FLAZASULFURON

1 Toxicology and metabolism

Absorption, distribution, excretion and metabolism in mammals

Rate and extent of absorption:	Rapid (90%) at low doses (based on urinary and biliary excretion), in rats.
Distribution:	Widely distributed.
Potential for accumulation:	No evidence for accumulation
Rate and extent of excretion:	Mainly for urine 75%-90% (within 7 days) in males and females respectively.
Toxicologically significant compounds:	Parent compound and metabolites: ADMP, DTPP, DTPU , TPSA.
Metabolism in animals:	Limited up to 30%-60% excreted as parent compounds in urine. 1) intramolecular rearrangement; 2) cleavage at sulfonylurea bridge; 3) oxidation; 4) conjugation.

Acute toxicity

Rat LD ₅₀ oral:	>5000mg/kgbw/day (m/f)
Rat LD ₅₀ dermal:	>2000mg/kgbw/day (m/f)
Rat LC ₅₀ inhalation:	> 5.99 mg/l (whole-body).
Skin irritation:	Non-irritant.
Eye irritation:	Non-irritant.
Skin sensitization (test method used and result):	Non sensitiser (Buehler and Maximisation tests).

Short term toxicity

Target / critical effect:	Liver (centrolobulillar hepatocyte hypertrophy).
Lowest relevant oral NOAEL / NOEL:	2 mg/kg bw/day, 13-week dogs and 1-year dogs

Lowest relevant dermal NOAEL / NOEL: >1000mg/kgbw/day (rabbits, 21-days).

Lowest relevant inhalation NOAEL / NOEL: No data. Not required.

Genotoxicity

No genotoxic potential.

Long term toxicity and carcinogenicity

Target / critical effect:

Liver (centrolobulillar hypertrophy) in mice and kidney (chronic nephropathy) in rats.

Lowest relevant NOAEL:

1.3mg/kg bw/day: 2-years rats.

Carcinogenicity:

No evidence for carcinogenic potential.

Reproductive toxicity

Target / critical effect - Reproduction:

Decrease pups weights at parental toxic doses. No effects on reproduction.

Lowest relevant reproductive NOAEL / NOEL:

Reproduction NOAEL= 653 mg/kgbw/day.

Pups NOAEL= 240 mg/kgbw/day (2000ppm).

Target / critical effect - Developmental toxicity:

Developmental effects at maternal toxic doses (foetal mortality, reduced foetal weight, skeletal variations) in rats.

Lowest relevant developmental NOAEL / NOEL:

100 mg/kgbw/day.

Delayed neurotoxicity

No data. No concern from other studies.

Other toxicological studies

Acute oral toxicity of metabolites in mice

ADMP LD₅₀ = 737/1073 mg/kgbw/day (m/f)

DTPU LD₅₀ = 2417/1847 mg/kgbw/day (m/f)

DTPP LD₅₀ >5000 mg/kgbw/day (m/f)

HTPP LD₅₀ >8450 mg/kgbw/day (m/f)

TPSA LD₅₀ = 1975/1727 mg/kgbw/day (m/f)

Genotoxicity tests of metabolites:

DTPU, DTPP and TPSA, which appear in groundwater at concentrations higher than 0.1 µg/L, are considered as of not genotoxicity concern.

2-weeks study in rats: Increase in deposition of hyaline droplets in proximal tubular cells of kidney.

Medical data

New substance. Limited information.

Summary

	Value	Study	Safety factor
ADI:	0.013 mg/kg bw	2yr study, rat,	100
AOEL systemic:	0.02 mg/kg bw/day	90d study, 1- year dog	100
AOEL inhalation:	Not required	Not required	Not required
AOEL dermal:	Not required	Not required	Not required
ARfD (acute reference dose): (if ARfD is required, please provide also information on dietary intake for children, e.g. NESTI)	Not allocated. Not necessary.		

Dermal absorption

10% assumed based on physical and chemical properties.

2 Fate and behaviour in the environment

2.1 Fate and behaviour in soil

Route of degradation

Aerobic:

Mineralization after 100 days:

2 to 5 %

Non-extractable residues after 100 days:

5 to 12 %

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

DTPU 62.5% (92 days), TPSA 23.7 % (91 days),
DTPP 7.5 % (276 days)

Supplemental studies

Anaerobic:

Only a flooded study has been presented. Similar degradation route was observed.

Soil photolysis:

DT₅₀ = 0.5 days (1 day in darkness). The same metabolites were observed (DTPU and DTPP).

Remarks:

No remarks

Rate of degradation

Laboratory studies

DT₅₀lab (20 °C, aerobic):

indoors 9-265 days, n=5, r>0.99 except for 265 days.
outdoors(15.8 + 3.7°C) 4-12 days, n=3 r >0.95

Metabolites:

DTPU 105-377 days
DTPP 117-904 days
TPSA 245-1165 days

DT₉₀lab (20 °C, aerobic):

indoors = not available
outdoors (15.8 + 3.7°C) 17-95 days n=3

DT₅₀lab (10 °C, aerobic):

indoors = 396 days, n=1.
DT₅₀ has been extrapolated

DT₅₀lab (20 °C, anaerobic):

Not available. 13-19 days in flooded soils.

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

DT _{50f} : France, Germany, Italy, Spain 2-18 days, n= 5, r >0.95 Maximum concentrations of metabolites: DTPU: 0.0123 mg/kg (0-10 cm depth), soil FR01 at day 60 after treatment. DTPP: 0.0162 mg/kg (0-10 cm depth), soil FR01 at day 120 after treatment. TPSA: 0.0141 mg/kg (0-10 cm depth), soil FR01 at day 0 after treatment.

DT_{90f} from soil dissipation studies:

DT _{90f} : France, Germany, Italy, Spain 10-100 days, n= 5, r>0.95

Soil accumulation studies:

No soil accumulation is expected.

Soil residue studies:

No data available

Remarks:

e.g. effect of soil pH on degradation rate

No remarks

Adsorption/desorptionK_f / K_{oc}:

30-100, 4 soils OM range = 0.8 - 4.7%, pH 5.5 - 7.5

K_d:

0.31-0.95

pH dependence:

No

Mobility**Laboratory studies:**

Column leaching:

8-86% radioactivity in the leachate. 80-90% is parent compound (column size: 40 cm long, inner diameter 5 cm, cross-sectional area 19.6 cm ²)

Aged residue leaching:

Aging time: 30 days. 7-14% radioactivity in the leachate. 90% is parent compound. No data of the concentration in the aged soil prior to the leaching.

Field studies:

Lysimeter/Field leaching studies:

No data available

Method of calculation and type of study (e.g. Modelling, monitoring, lysimeter)

FOCUS Scenarios. PELMO model (v. 3.21, FOCUS PELMO v. 2.2.2)

Application rate

Citrus: Single application 50 g as/ha Vines: Single application 50 g as/ha Olives: Single application 13.3 g as/ha

PEC(gw)

Maximum concentration (active substance) ($\mu\text{g/l}$)	Citrus: <0.001 – 0.076 (80th percentile) Vines: <0.001 – 0.029 (80th percentile) Olives: <0.001 – 0.006 (80th percentile)
Average annual concentration (active substance) ($\mu\text{g/l}$)	<<0.1 $\mu\text{g/l}$
Maximum concentration (metabolites) ($\mu\text{g/l}$)	Citrus: DTPU: 0.355 - 1.510 (80th percentile) DTPP: 0.128 - 0.522 (80th percentile) TPSA: 0.530 - 1.036 (80th percentile) Vines: DTPU: 0.398 - 2.163(80th percentile) DTPP: 0.143 - 0.827 (80th percentile) TPSA: 0.615 - 2.193 (80th percentile) Olives: DTPU: 0.157 - 0.722 (80th percentile) DTPP: 0.107 - 0.360(80th percentile) TPSA: 0.177 - 0.704 (80th percentile)
Average annual concentration (metabolites) ($\mu\text{g/l}$)	Citrus: DTPU: 0.294 – 1.214 DTPP: 0.109 – 0.433 TPSA: 0.445 – 0.708 Vines: DTPU: 0.323 – 1.687 DTPP: 0.118 – 0.646 TPSA: 0.518 – 2.015 Olives: DTPU: 0.128 – 0.546 DTPP: 0.086 – 0.306 TPSA: 0.150 – 0.586
Remarks:	DTPU, DTPP and TPSA are of no toxicological concern. DTPP, DTPU and TPSA were assessed according to all the criteria recommended in the step by step procedure for determination of the relevant metabolites (doc Sanco/221/2000 rev 10). On this basis, it can be concluded that DTPP, DTPU and TPSA are not relevant.

2.2 Fate and behaviour in water

Abiotic degradation

Hydrolytic degradation:

pH 4: 0.5 days, 25°C
pH 5: 2.6 days, 25°C
pH 7: 11 days, 25°C
pH 9: 8.8 days, 25°C
Calculated using the Arrhenius equation from studies at 22° C and 37 ° C ($r^2 > 0.99$)

Major metabolites:

DTPU is the major metabolite (pH 4,5 and 7)
DTPP is the major metabolite at pH 9.

Photolytic degradation:

Stable to direct photolysis. No differences between the light and dark control during the first week.

Major metabolites:

Stable

Biological degradation

Readily biodegradable:

No data available

Water/sediment study:

DT₅₀ water:

14 –15.6 days

DT₉₀ water:

52 – 73 days

DT₅₀ whole system:

23 days

DT₉₀ whole system:

76 –98 days

Distribution in water / sediment systems (active substance)

10-15% AD in sediments after 10-30 days
Maximum sediment concentration: 15.7% AD (at 10 days)
Water phase concentration at 10 days: 51.6 % AD.

Distribution in water / sediment systems (metabolites)

DTPU 16.3% AD in sediment at 100 days
HTPP 29% AD in sediment at 100 days
DTPU 27.7% AD in water phase at 21 days

Accumulation in water and/or sediment:

No data available. See water/sediment

Degradation in the saturated zone No data available.

Remarks:

No remarks

2.3 Fate and behaviour in air

Volatility

Vapour pressure:

Vapor pressure at 25°C, 35°C and 45°C was determined to be $< 1.33 \times 10^{-5}$ Pa. Purity 99.8%.

Henry's law constant:

2.5799×10^{-6} Pa m ³ mol ⁻¹

Photolytic degradation

Direct photolysis in air:

No data submitted

Photochemical oxidative degradation in air
DT₅₀:

Atkinson calculation: DT ₅₀ 0.6 hours

Volatilisation:

from plant surfaces: No data submitted from soil: No data submitted

Remarks:

No remarks

3 Ecotoxicology

Terrestrial Vertebrates

Acute toxicity to mammals:

Rat LD50 >5000 mg/kg b.w.
Formulated product: Rat LD50 = 1216 mg a.i./kg b.w.

Acute toxicity to birds:

Bobwhite quail LD50 >2000 mg/kg b. w.
Formulated product: Japanese quail LD50 = 995 mg a.i./kg b.w.

Dietary toxicity to birds:

Bobwhite quail and Mallard duck LC50 > 5620 ppm

Reproductive toxicity to birds:

Bobwhite quail and Mallard duck NOEC 1000 ppm

Short term oral toxicity to mammals:

Rat 13weeks NOEL = 200 ppm (11.7 mg/kg/day)
Rat teratogenicity NOEL = 100 mg/kg bw/day

Aquatic Organisms

Acute toxicity fish:

Species	Test substance	Toxicity (mg/ l)	Endpoint
<i>Oncorhynchus mykiss</i>	technical	22	96h LC50
<i>Oncorhynchus mykiss</i>	TPSA	>100	96h LC50
<i>Oncorhynchus mykiss</i>	DTPU	122	96h LC50
<i>Oncorhynchus mykiss</i>	DTPP	>82	48h EC50
<i>Oncorhynchus mykiss</i>	technical	5	21d NOEC
No study required log Kow = 1.30			
<i>D.magna</i>	technical formulated product	>106 >25 a.s.	48h EC50
<i>D.magna</i>	TPSA	60.2	48h EC50
<i>D.magna</i>	DTPU	>200	48h EC50
<i>D. magna</i>	DTPP	166	48h EC50
<i>Chironomus riparius</i>	DTPU	100	48h NOEC
<i>Chironomus riparius</i>	HPP	100	48h NOEC
<i>D.magna</i>	technical	6.25	21 days NOEC
<i>Pseudokirchneriella subcapitata</i>	formulated	0.014 a.s	72 hours EC50

Long term toxicity fish:

Bioaccumulation fish:

Acute toxicity invertebrate:

Chronic toxicity invertebrate:

Acute toxicity algae:

	<i>Species</i>	<i>Test substance</i>	<i>Toxicity (mg/l)</i>	<i>Endpoint</i>
Chronic toxicity algae:	<i>Anabaena flos-aquae</i>	Technical	0.005	96h NOEC
	<i>Pseudokirchneriella subcapitata</i>	Technical	0.045	96h NOEC
	<i>Scenedesmus subspicatus</i>	DTPP	37	72 h NOEC
	<i>Scenedesmus subspicatus</i>	DTPU	9	72 h NOEC
	<i>Scenedesmus subspicatus</i>	TPSA	>100.1	72 h NOEC
	Chronic toxicity sediment dwelling organism:	<i>Chironomus riparius</i>	technical	0.1
Acute toxicity aquatic plants:	<i>Lemna gibba</i>	Technical	0.00004/ 0.00002	7d EC50/ NOEC
	<i>Lemna gibba</i>	Technical	0.0007	7d EC50

Honeybees

Acute oral toxicity:

LD50 technical >100 µg/bee LD50 formulation > 178.7 µg/bee

Acute contact toxicity:

LD50 technical >100 µg/bee LD50 formulation >100 µg/bee

Other arthropod species

<i>Test species</i>	Status	Dose (kg as/ha)	Test substance	% Effect; End point
<i>Typhlodromus pyri</i>	Adults	0.02	Technical	11%; Beneficial capacity
<i>Poecilus cupreous</i>	Adults	0.05	Technical	No effects; Mortality, behaviour, food consumption
<i>Pardosa</i> sp.	Non reproductive adults	0.05	Technical	No effects; Mortality, behaviour, food consumption
<i>Aphidius rhopalosiphi</i> *	Adults	0.05	25 % WG formulated	No effects; Mortality, reproduction
<i>Typhlodromus pyri</i> *	Protonymphs (24-48 h old)	0.05	25 % WG formulated	16.3%; Beneficial capacity

Earthworms

Acute toxicity:

Technical : LC50 >15.75 ppm Metabolites: DMP, DTPP, DTPU, TPSA, HTPP 7d LC50 >1250 ppm

Reproductive toxicity:

No data submitted

Soil micro-organisms

Nitrogen mineralization:

No relevant effects for 10x the a.r.

Carbon mineralization:

No relevant effects for 10x the a.r.

APPENDIX III**FLAZASULFURON**

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
IIA, 1.11.1	Holly A. Weber	2003	Group A-Product Chemistry Analysis of Flazasulfuron Midwest Research Institute, Kansas City, Missouri MRI Project No.: 310260.1.024 GLP/GEP: yes Published: no
IIA / 2.15	Sweetapple, G.G	2000	SL-160 (TGAI) Oxidising properties Ishihara Sangyo Kaisha, Ltd. Reort No. 011950-1 Ricerca GLP/GEP: yes Published: no
IIIA / 2.7.1	Schmiedel, U.	1998	Determination of the storage stability of SL-160 25% WG RCC Umweltchemie GmbH & Co. Report No. 610492 GLP/GEP: yes Published: no
IIIA / 2.8.6.1	Mirbach, M.J.	1999	SL-160 25% WG: Attrition resistance of granules RCC Umweltchemie GmbH & Co. Report No. 747415 GLP/GEP: yes Published: no
IIA/4.2.1	Andreas Wais	2000	Validation of the residue analytical method for SL-160 in vine (RAC grapes) RCC report No.: 763964 GLP/GEP: yes Published: no
IIA/4.2.2	Ullrich-Mitzel, A.	1996	Validation of analytical method for determination of residues of SL-160 and its metabolites DTPP, DTPU, and TPSA in soil. ISK, RCC 627625 GLP/GEP: yes Published: no

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/4.2.3	Wais, A.	1999	Validation of an analytical method for the determination of SL-160, DTPU, TPSA in surface water. GLP/GEP: yes Published: no
IIA, 4.2.4	Andreas Wais	1999	Validation of the residue analytical method for SL-160 in air RCC report No.: 727705 GLP/GEP: yes Published: no

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 /5.2.6	Hideo Ueda, D.V.M.	1998	SL-160 technical: Dermal sensitization study in Guinean Pigs. Maximization test Company: XXX StudyNo.: IET96-0090 GLP/GEP: yes Published: no
IIA / 7.1.6	Hideo Ueda, D.V.M.	1998	SL-160 25% WG: Dermal sensitization study in Guinean Pigs. Maximization test Company: XXX StudyNo.: IET96-0091 GLP/GEP: yes Published: no
IIA, 5.8.1	Masumori, S.	2003	Gene mutation assay of DTPU (SL-160 metabolite) with mouse lymphoma cells (MLA) Report No. 6543 (309-005) GLP/GEP: yes Published: no
IIA, 5.8.1	Wollny, H. E.	2003	Cell mutation assay at the thymidinr kinase locus (TK+/-) in mouse lymphoma cells L5178Y cells with DTPU (SL-160 metabolite) Report No. 778503 GLP/GEP: yes Published: no
IIA, 5.8.1	Ajimi, S.	2003	In vitro mammalian cell gene mutation test of TPSA (SL-160 metabolite) using mouse lymphoma cells Report No. K22-0003 GLP/GEP: yes Published: no

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, 5.8.1	Ajimi, S.	2003	Chromosome aberration test of DTPU (SL-160 metabolite) using cultured mammalian cells Report No. K06-0945 GLP/GEP: yes Published: no
IIA, 5.8.1	Ajimi, S.	2003	Chromosome aberration test of DTPP (SL-160 metabolite) using cultured mammalian cells Report No. K06-0946 GLP/GEP: yes Published: no
IIA, 5.8.1	Ajimi, S.	2003	Chromosome aberration test of TPSA (SL-160 metabolite) using cultured mammalian cells Report No. K06-0947 GLP/GEP: yes Published: no
IIA, 5.8.1	Honarvar, N.	2003	Micronucleus assay in bone marrow cells of the mouse with DTPP (SL-160 metabolite) Report No. 765802 GLP/GEP: yes Published: no
IIA, 5.8.1	Honarvar, N.	2003	Micronucleus assay in bone marrow cells of the mouse with TPSA (SL-160 metabolite) Report No. 765803 GLP/GEP: yes Published: no
IIA,5.8.1	ISK Bioscience	2003	FLAZASULFURON (SL-160) AND ITS METABOLITES DTPU, DTPP, TPSA. Sequential assessment on the toxicological relevance of metabolites in groundwater based on the EU working document Sanco/221/2000- Rev 10 (25 February 2003) GLP/GEP: no Published: no

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
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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 / 6.5.1	Wais, A.	1998	Processing of olives to olive oil and determination of SL-160 residues in olives, olive oil and press cake meal following application of SL-160 25% WG formulated product in groves in Italy, 1997 ReportNo.:688072 RCC Ltd Environmental Chemistry & PharamanalyticsDivision SubmittedinNovember GLP/GEP:yes Published: no
IIA / 6.5.1	Wais, A.	1998	Processing of olives to olive oil and determination of SL-160 residues in olives, olive oil and press cake meal following application of SL-160 25% WG formulated product in groves in Spain, 1997 ReportNo.:688061 RCC Ltd Environmental Chemistry & PharamanalyticsDivision GLP/GEP:yes Published: no
IIA / 6.3	Wais, A.	1999	Determination of SL-160 residues in oranges following application of SL-160 25% WG formulated product in orange tree groves in Italy and Spain, 1998. ReportNo.:711540 RCC Ltd Environmental Chemistry & Pharamanalytics Division GLP/GEP:yes Published: no
IIA / 6.3	Wais, A.	1999	Determination of SL-160 residues in oranges & mandarins following application of SL-160 25% WG formulated product in citrus tree groves in Greece, 1998. ReportNo.:711538 RCC Ltd Environmental Chemistry & Pharamanalytics Division GLP/GEP:yes Published: no

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 / 9.2.1	James J. McFadden, Ph. D	2000	James J. McFadden, Ph. D Re-calculation of Maximum PEC Values for SL-160 (Flazasulfuron) metabolites Ricerca – Report No.: 01224 GLP/GEP: no Published: no

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 / 7.2.2	Leyes, G.A.	2000	Estimation of the atmospheric oxidation of DTPU, DTPP and TPSA, the environmental metabolites of SL-160 Ricerca – Report No.: 12247-1 GLP/GEP: No Published: No
IIA / 9.2.1	James J. McFadden, Ph.D.	2002	Evaluation of SL-160 Leaching Potential for Citrus, Vines and Olives According to FOCUS Scenarios. RICERSA Biosciences PECGW/SL-160,metabolites Report No.013427-6 GLP/GEP: No Published: No

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 / 8.2.1	Peither A.	1998	Acute toxicity of DTPP to Rainbow Trout (<i>Onchorhynchus mykiss</i>) in a 96-hour statictest RCCStudyNo.:692223 GLP/GEP: yes Published: no
IIA / 8.2.1	Peither A.	1998	Acute toxicity of DTPU to Rainbow Trout (<i>Onchorhynchus mykiss</i>) in a 96-hour statictest RCCStudyNo.:692201 GLP/GEP: yes Published: no
IIA / 8.2.1	Peither A.	1998	Acute toxicity of TPSA to Rainbow Trout (<i>Onchorhynchus mykiss</i>) in a 96-hour static test RCC Study No.: 692188 GLP/GEP: yes Published: no
IIA / 8.2.7	Memmert, U.	2000	Effects of SL-160 on the development of sediment-dwelling larvae of Chironomus riparius in a water-sediment system RCC Report No.: 731823 GLP/GEP: yes Published: no
IIA / 8.2.7	Memmert, U.	1999	Acute toxicity of HTPP to first instar larvae of Chironomus riparius RCC Report No.: 731878 GLP/GEP: yes Published: no

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 / 8.2.7	Memmert, U.	1999	Memmert, U. Acute toxicity of DTPU to first instar larvae of Chironomus riparius RCC Report No.: 731845 GLP/GEP: yes Published: no
IIA / 8.2.8	Memmert, U.	1999	Memmert, U. Toxicity of ¹⁴ C-SL-160 (P) to the aquatic higher plant Lemma gibba in a 7-day static growth inhibition test RCC Report No.: 728820 GLP/GEP: yes Published: no
IIIA / 10.5.1	Moll, M.	1999	Effects of SL-160 25 WG on the parasitoid Aphidius rhopalosiphii (Hymenoptera, Aphidiidae) – Extended laboratory study Report No.: 496002 GLP/GEP: yes Published: no
IIIA / 10.5.1	Moll, M.	2000	Side effects of Flazasulfuron 25% WG on the predatory mite Typhlodromus pyri (Acari, Phytoseiidae) on glass plates Report No.: TPE.01/2000 GLP/GEP: yes Published: no

APPENDIX IV

FLAZASUFURON

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/ha min max	water l/ha min max	kg as/ha min max		
Grapes	Europe (e.g: France , Italy, Spain, Portugal)	Katana 25% WG	F	annual grasses, dicots	WG	250 g/kg	low volume spraying under the rows	early post- emer- gence	1	75 days	0.025- 0.0125	200-400	0.05 max	75	timing : Spring (February - April)
Citrus	Europe (e.g: Spain, Italy)	Katana 25% WG	F	annual grasses, dicots	WG	250 g/kg	low volume spray broad-cast or under the rows	early post- emer- gence	1	30 days	0.025 to 0.0125	200-400	0.05 max	45	timing : Summer (June – August)

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		
Olives	Europe	Katana 25% WG	F	annual grasses, dicots	WG	250 g/kg	low volume spray band along the base of the trees	pre- and early post- emer- gence	1	120 days	0.025 to 0.0125	200-400	0.013 max	45	timing : Autumn – Spring (October – March)

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