FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

FLAZASULFURON

1-(4,6-dimethoxypyrimidin-2-yl)-3-(3-trifluoromethyl-2-pyridylsulphonyl)urea

FOOD AND AGRICULTURE ORGANIZATION of THE UNITED NATIONS

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Compliance with the specifications does not constitute an endorsement or warranty of the fitness of a particular pesticide for a particular purpose, including its suitability for the control of any given pest, or its suitability for use in a particular area. Owing to the complexity of the problems involved, the suitability of pesticides for a particular purpose and the content of the labelling instructions must be decided at the national or provincial level.

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[1] This disclaimer applies to all specifications published by FAO.

INTRODUCTION

FAO establishes and publishes specifications* for technical material and related formulations of agricultural pesticides, with the objective that these specifications may be used to provide an international point of reference against which products can be judged either for regulatory purposes or in commercial dealings.

Since 1999 the development of FAO specifications follows the **New Procedure**, described in the 5th edition of the "Manual on the development and use of FAO specifications for plant protection products" (FAO Plant Production and Protection Page No. 149). This **New Procedure** follows a formal and transparent evaluation process. It describes the minimum data package, the procedure and evaluation applied by FAO and the Experts of the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS). [Note: prior to 2002, the Experts were of the FAO Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent, which now forms part of the JMPS, rather than the JMPS.]

FAO Specifications now only apply to products for which the technical materials have been evaluated. Consequently from the year 2000 onwards the publication of FAO specifications under the **New Procedure** has changed. Every specification consists now of two parts namely the specifications and the evaluation report(s):

PART ONE: **The Specification** of the technical material and the related formulations of the plant protection product in accordance with chapter 4, 5 and 6 of the 5th edition of the "Manual on the development and use of FAO specifications for plant protection products".

PART TWO: **The Evaluation Report(s)** of the plant protection product reflecting the evaluation of the data package carried out by FAO and the JMPS. The data are to be provided by the manufacturer(s) according to the requirements of Appendix A, Annex 1 or 2 of the "Manual on the development and use of FAO specifications for plant protection products" and supported by other information sources. The Evaluation Report includes the name(s) of the manufacturer(s) whose technical material has been evaluated. Evaluation reports on specifications developed subsequently to the original set of specifications are added in a chronological order to this report.

FAO specifications under the **New Procedure** do not necessarily apply to nominally similar products of other manufacturer(s), nor to those where the active ingredient is produced by other routes of manufacture. FAO has the possibility to extend the scope of the specifications to similar products but only when the JMPS has been satisfied that the additional products are equivalent to that which formed the basis of the reference specification.

Specifications bear the date (month and year) of publication of the current version. Dates of publication of the earlier versions, if any, are identified in a footnote. Evaluations bear the date (year) of the meeting at which the recommendations were made by the JMPS.

*NOTE: publications are available on the internet at http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/ or in hardcopy from the Plant Protection Information Officer.

PART ONE

SPECIFICATIONS

FLAZASULFURON

FLAZASULFURON

INFORMATION

ISO common name

Flazasulfuron (ISO 1750 published)

Synonym

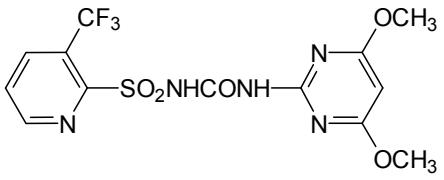
SL-160

Chemical name(s)

IUPAC 1-(4,6-dimethoxypyrimidin-2-yl)-3-(3-trifluoromethyl-2-pyridylsulphonyl)urea

CA 2-pyridinesulfonamide,N-[[(4,6-dimethoxy-2-pyridimidinyl)amino] carbonyl]-3-(trifluoromethyl)

Structural formula



Molecular formula

$C_{13}H_{12}F_3N_5O_5S$

Relative molecular mass

407.36

CAS Registry number

104040-78-0

CIPAC number

595

Identity tests

Retention time in HPLC and UV spectrum

FLAZASULFURON TECHNICAL MATERIAL

FAO Specification 595/TC (April 2013*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (595/2010). It should be applicable to relevant products of these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (595/2010) as PART TWO forms an integral part of this publication.

1 Description

The material shall consist of flazasulfuron together with related manufacturing impurities, in the form of a granular cream coloured solid having a strong lawn fertiliser odour, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (595/TC, Note 1)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 **Flazasulfuron content** (595/TC, Note 1)

The flazasulfuron content shall be declared (not less than 940 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

Note 1 The reversed phase HPLC method (CIPAC/4831) for the determination of flazasulfuron in TC and WG formulations was adopted as provisional method by CIPAC in 2012. Prior to its publication in one of the next Handbooks, copies of the method may be obtained through the CIPAC prepublishment scheme, http://www.cipac.org/cipacpub.htm

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/

FLAZASULFURON WATER DISPERSIBLE GRANULES

FAO Specification 595/WG (April 2013*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose name is listed in the evaluation report (595/2010). It should be applicable to relevant products of these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report (595/2010) as PART TWO forms an integral part of this publication.

1 **Description**

The material shall consist of an homogeneous mixture of technical flazasulfuron, complying with the requirements of the FAO specification 595/TC (April 2013), in the form of a brownish granular solid with a cinnamon like odour, together with carriers and any other necessary formulants. It shall be in the form of rod shaped granules for application after disintegration and dispersion in water. The formulation shall be dry, free-flowing, essentially non-dusty, and free from visible extraneous matter and hard lumps.

2 **Active ingredient**

2.1 **Identity tests** (595/WG, Note 1)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 **Flazasulfuron content** (595/WG, Note 1)

The flazasulfuron content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the following tolerances:

Declared content in g/kg	**Tolerance**
above 100 up to 250	± 6 % of the declared content
above 250 up to 500	±5 % of the declared content
Note: In each range the upper limit is included	

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-new/en/

3 Physical properties

3.1 **Wettability** (MT 53.3)

The formulation shall be completely wetted in 5 seconds, without swirling.

3.2 **Wet sieve test** (MT 185)

Maximum: 0.2 % retained on a 75 µm test sieve.

3.3 **Degree of dispersion** (MT 174)

Dispersibility: minimum 97 % after 1 minute of stirring.

3.4 **Suspensibility** (MT 184) (Notes 2 & 3)

A minimum of 70 % shall be in suspension after 30 min in CIPAC Standard Water D at 30 ± 2°C.

3.5 **Persistent foam** (MT 47.2) (Note 4)

Maximum: 5 ml after 1 minute.

3.6 **Dustiness** (MT 171) (Note 5)

Nearly dust-free

3.7 **Flowability** (MT 172)

At least 99 % of the formulation shall pass through a 5 mm test sieve after 20 drops of the sieve.

3.8 **Attrition resistance** (MT 178.2)

Minimum: 99.5 % attrition resistance.

4 Storage stability

4.1 **Stability at elevated temperature** (MT 46.3)

After storage at 54 ± 2°C for 14 days, the determined average active ingredient content must not be lower than 95% relative to the determined average content found before storage (Note 6) and the formulation shall continue to comply with the clauses for:

- wet sieve test (3.2),
- degree of dispersion (3.3),
- suspensibility (3.4),
- dustiness (3.6),
- attrition resistance (3.8).

Note 1 The reversed phase HPLC method (CIPAC/4831) for the determination of flazasulfuron in TC and WG formulations was adopted as provisional method by CIPAC in 2012. Prior to its publication in one of the next Handbooks, copies of the method may be obtained through the CIPAC prepublishment scheme, http://www.cipac.org/cipacpub.htm

Note 2 The formulation should be tested at the highest and lowest rates of use recommended by the supplier, provided this does not exceed the conditions given in methods MT 184.

Note 3 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. In case of dispute, chemical assay shall be the "referee method".

Note 4 The mass of sample to be used in the test should be specified at the highest rate recommended by the supplier. The test is to be conducted in CIPAC standard water D.

Note 5 Measurement of dustiness must be carried out on the sample "as received" and, where practicable, the sample should be taken from a newly opened container, because changes in the water content of samples may influence dustiness significantly. The optical method, MT 171.2, usually shows good correlation with the gravimetric method, MT 171.1, and can, therefore, be used as an alternative where the equipment is available. Where the correlation is in doubt, it must be checked with the formulation to be tested. In case of dispute the gravimetric method shall be used.

Note 6 Analysis of the formulation, before and after the storage stability test, should be carried out concurrently (i.e. after storage) to reduce analytical error.

PART TWO

EVALUATION REPORTS

FLAZASULFURON

FLAZSULFURON

FAO EVALUATION REPORT 595 / 2010

Recommendations

The meeting recommended that:

(i) the proposed specifications for flazasulfuron TC and WG, proposed by ISK Biosciences, as amended, should be adopted by FAO, subject to the availability of a collaboratively validated analytical method

Appraisal

The data for flazasulfuron were evaluated in support of new FAO specifications. ISK Biosciences provided the draft specification and the supporting data in 2009.

Flazasulfuron is no longer under patent.

Flazasulfuron has not been evaluated by the FAO/WHO JMPR or WHO/IPCS. It was evaluated by the European Commission in 2004 (rapporteur member state Spain) and by US EPA in 2007.

The confidential data presented by ISK Biosciences for the manufacturing process, impurities and batch analysis are identical to those submitted for registration in the European Union and in Germany.

The results of a small scale study for the validation of the analytical method for determination of flazasulfuron was presented at the CIPAC meetings in 2010 and 2011. In 2012 a full scale trial was available and the method was adopted as provisional by CIPAC. Flazasulfuron is determined by isocratic reversed phase HPLC on an ODS column, UV-detection at 260 nm and external standard calibration. Identity tests rely on comparison of retention time in HPLC and UV spectra, but other methods like IR- spectroscopy and NMR spectroscopy are available as well.

The technical material is a granular cream coloured solid with a melting range in DSC from 147 to 150 °C. Pure flazasulfuron is a white powder with a melting point of 180 °C. The vapour pressure is low and the water solubility is strongly dependent on pH, with increasing solubility with higher pH values. The octanol/water partition coefficient is low, indicating that flazasulfuron shows not tendency for bioaccumulation.

As with other sulfonylurea herbicides, the protons at the sulfonylurea bridge are easily removed (pK_a for flazasulfuron being 4.37, the pK_a for the second dissociation step is not given by the proposer). Flazasulfuron is therefore a weak acid.

Flazasulfuron is readily hydrolysed at 25 °C at pH below 7. Flazasulfuron is initially stable to photolysis. Hydrolysis is the mechanism of reaction for the first seven days. After seven days, the photoproduct or a component in the polar fraction acts as a photosensitizer and accelerates the photodegradation. The half-life during the first seven days is about 16 days

(which is comparable to hydrolysis half-life) and the half-life from 7 to 30 days is approximately 7.5 days.

The draft specification contained a clause for residual water was as relevant impurity for TC and WG. After re-evaluation the proposer decided that water is no relevant impurity in WG. In the TC the content of water was only based on the 5 batch analysis data submitted in the EU evaluation process, so the Meeting does not consider water is relevant in TC either.

The Meeting was provided with commercially confidential information of the 5-batch analytical data on the purity and impurities ≥1 g/kg. Mass balances were high (98.3 - 99.7 %) and there were no unidentified impurities. Methods of analysis for the active ingredient was a HPLC method which later on was collaboratively validated and adopted by CIPAC. Most the impurities were analysed by HPLC-UV, whereas Karl Fischer titration was used for deterniation of water. All in-house methods were adequately validated.

According to the procedure described in Annex J of the FAO/WHO Manual, ADMP (2-amino-4,6-dimethoxypyrimidine) could be considered as potential relevant impurity. Based on the LD_{50} (oral, mice), the relative hazard of ADMP is $RelHaz_{imp}$ = 5000/737 = 6.78 and the MTIHaz is 1.433, which is above the trigger-value of 1.1. The maximum tolerable value for ADMP $\%Imp_{maxaccept}$ would be 1.39 %, but the maximum value specified by the proposer is significantly lower than the level considered accpeptable by the contribution to the overall hazard.
However, bearing in mind that ADMP is a major metabolite of flazasulfuron and based on the very low toxicity of flazasulfuron itself, the Meeting concluded that ADMP does not qualify as a relevant impurity.

The proposed specifications for TC and WG do comply with the requirements of the FAO/WHO Manual, November 2010 revision of the first edition.

In the WG specification the proposed method for wet sieve test is MT 59.3 and for the determination of suspensibility MT 15.1 and MT 168. In both cases, updated MT methods are available, so the Meeting proposed to replace MT 59.3 by MT 185 (as stated in the specification guideline for WG) and MT 15.1 and MT 168 by MT 184. The proposer stated that the proposed values were determined using the methods referenced in the draft specification but accepted to mention only the updated methods. The Meeting questioned the necessarity to specify a pH value for WG formulations and the proposer agreed to delete it.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 595 / 2010

Identity of the active ingredient

ISO common name

Flazasulfuron (ISO 1750 published)

Synonym

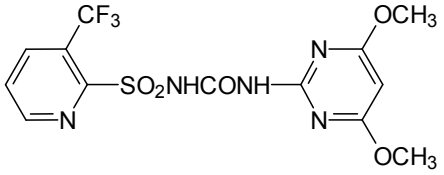
SL-160

Chemical name(s)

IUPAC 1-(4,6-dimethoxypyrimidin-2-yl)-3-(3-trifluoromethyl-2-pyridylsulphonyl)urea

CA 2-pyridinesulfonamide,N-[[(4,6-dimethoxy-2-pyridimidinyl)amino]carbonyl]-3-(trifluoromethyl)

Structural formula



Molecular formula

$C_{13}H_{12}F_3N_5O_5S$

Relative molecular mass

407.36

CAS Registry number

104040-78-0

CIPAC number

595

Identity tests

Retention time in reversed phase HPLC and UV spectrum

Table 1. Physico-chemical properties of pure flazasulfuron

<table>
<tr><th>Parameter</th><th>Value(s) and conditions</th><th>Purity %</th><th>Method reference (and technique if the reference gives more than one)</th><th>Study number</th></tr>
<tr><td>Vapour pressure</td><td>< 1.33 x 10^{-5} Pa at 25°C – 45 °C</td><td>99.8%</td><td>EEC Method A4. Gas saturation (Gas chromatography) .</td><td>4039-91-0399-AS-001</td></tr>
<tr><td>Melting point.</td><td>180 °C</td><td>99.7%</td><td>EEC Method A.1, DSC. Guideline 537-86 (1992).</td><td>4594-96-0188-AS-001</td></tr>
<tr><td>Temperature of decomposition</td><td>No sublimation. Decomposition initiated at 181.5 ºC as evidenced by gas evolution.</td><td>99.7%</td><td>Capillary tube observation.</td><td>4594-96-0188-AS-001</td></tr>
<tr><td>Solubility in water</td><td>0.027 g/l at 25 °C at pH 5
2.1 g/l at 25 °C at pH 7</td><td>99.8%</td><td>EEC Method A.6. Flask method with determination by liquid chromatography</td><td>4039-91-0400-AS-001</td></tr>
<tr><td>Octanol/water partition coefficient</td><td>log K_{OW} = 1.30 at 25 °C pH 5
log K_{OW} < - 0.06 at pH 7</td><td>99.8%</td><td>40 CFR 158.190
EPA D, 63-11</td><td>4039-91-0401-AS-001</td></tr>
<tr><td>Hydrolysis characteristics</td><td>The half-lives (DT_{50} values = $t_{½}$ values) of the hydrolysis of Flazasulfuron (SL-160) in sterile buffer solution at different temperatures and pH conditions:
<table>
<tr><th>pH</th><th>22 °C</th><th>37 °C</th><th>25 °C (calculated)</th></tr>
<tr><td>4</td><td>0.78 d</td><td>2.65 h</td><td>11.5 h</td></tr>
<tr><td>5</td><td>3.9 d</td><td>14.67 h</td><td>2.6 d</td></tr>
<tr><td>7</td><td>17.34 d</td><td>64.66 h</td><td>11.3 d</td></tr>
<tr><td>9</td><td>13.48 d</td><td>44.66 h</td><td>8.8 d</td></tr>
</table></td><td>> 99.5 % (chemical)
> 98 % (radiochem.)</td><td>In-house
EPA 161-1
OECD 111</td><td>5564-92-0493-EF-001</td></tr>
<tr><td>Photolysis characteristics</td><td>Half-life at pH 7 and 22 °C:
8.9 d [^{14}C]SL-160 (P)
8.0 d [^{14}C] SL-160 (Pm)</td><td>> 99.5 % (chemical)
> 98 % (radiochem.)</td><td>In-house
EPA 161-2</td><td>5563-92-0492-EF-001</td></tr>
</table>

Dissociation characteristics	pK_a = 4.37 ± 0.08 (20 ± 1°C)	99.7%	In-house UV spectra method. OECD 112	4039-91-0404-AS-001
Solubility in organic solvents	0.5 ± 0.04 mg/L n-hexane 0.56 ± 0.014 g/l toluene 22.1 ± 0.54 g/l dichloromethane 4.2 ± 0.10 g/l methanol 22.7 ± 0.75 g/l acetone 6.9 ± 0.21 g/l ethyl acetate 0.20 ± 0.013 g/l n-octanol 8.7 ± 0.18 g/l acetonitrile at 25 ± 1°C	99.8%	EC Method A.6. Flask method with quantitation by liquid chromatography for n-hexane	4039-91-0400-AS-001

Table 2. Chemical composition and properties of flazasulfuron technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO. Mass balances were 98.3 – 99.7 %. No unknowns were identified in the 5 batch analysis.
Declared minimum flazasulfuron content	940 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities < 1 g/kg and maximum limits for them:	None
Stabilisers or other additives and maximum limits for them:	None

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC	150 °C	97-98.5	EEC Method A.1, Melting point apparatus. Guideline 537-86 (1992).	4039-92-0496-AS-001
Solubility in organic solvents	Not available, see values for pure a.i.	-	-	-

USES

Flazasulfuron belongs to the family of the sulfonylurea herbicides. Products containing flazasulfuron are used in agriculture in the root zone of grapevine, citrus and olive trees to control weeds like grasses. It is rapidly absorbed through leaves and roots of the weeds. It is translocated through the xylem and the phloem towards the meristemic zones. Flazasulfuron interferes with the acetolactate synthase (ALS), a key enzyme for branched-chain amino acids synthesis, resulting in cessation of cell division and plant growth.

FORMULATIONS AND CO-FORMULATED ACTIVE INGREDIENTS

The main formulation type available is WG, used as agricultural herbicide. The 25 WG formulation is registered and sold in many countries in the European Union, Japan, China, Korea, Taiwan and South Africa. Flazasulfuron is not co-formulated with other pesticides.

METHODS OF ANALYSIS AND TESTING

The method for the technical material and WG has been adopted by CIPAC as provisional CIPAC method in 2012.

Flazasulfuron is determined by isocratic reversed phase HPLC (column: Zorbax Eclipse XDB-C18, 5 µm, 250 x 4.6 mm i.d.) with water (0.05 % acetic acid) / acetonitrile (45:55, v/v) as mobile phase, UV-detection at 260 nm and external standard calibration.

The methods for determination of impurities are based on HPLC-UV.

Test methods for determination of physico-chemical properties of the technical active ingredient were EC and in-house-methods, while those for the formulations were CIPAC, as indicated in the specifications.

PHYSICAL PROPERTIES

The physical properties, the methods for testing them and the limits proposed for the WG formulation comply with the requirements of the FAO/WHO Manual, (2010 revision of the 1st edition).

CONTAINERS AND PACKAGING

No special requirements for containers and packaging have been identified.

EXPRESSION OF THE CONTENT OF THE ACTIVE INGREDIENT

The active ingredient is expressed as flazasulfuron

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Notes.

(i) The proposer confirmed that the toxicological and ecotoxicological data included in the summary below were derived from flazasulfuron having impurity profiles similar to those referred to in the table above.

(ii) The conclusions expressed in the summary below are those of the proposer, unless otherwise specified.

Table 3. Toxicology profile of flazasulfuron technical material, based on acute toxicity, irritation and sensitization

Species	Test	Purity % Note[2]	Duration and conditions	Result	Reference
Rat (males / females)	acute oral	96.3	Guidelines of Japanese MAFF in Japan (1985); FIFRA EPA in USA (1984); and OECD (1981) which is comparable to 92/69/EEC part B1; 14-day observation period; 2500 mg/kg bw or 5000 mg/kg bw	LD_{50} > 5000 mg/kg bw	87-0100
Mice (males / females)	acute oral	96.3	Guidelines of MAFF in Japan (1985); FIFRA EPA in USA (1984); and the OECD (1981) which is comparable to 92/69/EEC part B1; 14-day observation period; 2500 mg/kg bw or 5000 mg/kg bw; purity 96.3 %	LD_{50} > 5000 mg/kg bw	87-0101
Rat (males / females)	dermal	96.3	Guidelines of MAFF in Japan which is comparable to 92/69/EEC part B3; 14-day observation period ; 1000 or 2000 mg/kg bw ;	LD_{50} > 2000 mg/kg bw	87-0102
Rat (males / females)	inhalation	96.4	Guidelines 92/69/EEC part B2; 14-day observation period; 5.99 mg/L;	LC_{50} > 5.99 mg/L	87-0106
Rabbit (males / females)	skin irritation	97.3	Guideline US EPA FIFRA No 81-5, which is comparable to 92/69/EEC part B4; 72 hours observation period; 0.5 g;	Non-irritant	5490-92-0409-TX-001
Rabbit (males / females)	eye irritation	97.3	Guideline No 81-4 US EPA FIFRA, which is comparable to 92/69/EEC part B5; 72 hours observation period; 0.1 g;	Non-irritant	5489-92-0408-TX-001
Guinea pigs (males/females)	skin sensitisation	97.5	Guideline EPA FIFRA, No 81-6 US, which is comparable to 92/69/EEC part B6; 48 hours observation period; 0.4 g per site;	No dermal sensitization.	5488-92-0407-TX-001
Guinea pigs (females)	maximization test	97.5	US EPA Pesticide Assessment Guidelines Subdivision F, 81-6; 48 hours; 2.5, 50%;	No dermal sensitization.	96-0090

[2] Note: Purity is the content of pure active ingredient in the technical material, expressed as a percentage.

Table 4. **Toxicology profile of technical flazasulfuron based on repeated administration (sub-acute to chronic)**

Species	Test	Purity % Note[32]	Duration and conditions	Result	Reference
Mice (males/ females)	Oral subacute	97.3	Guidelines 92/ 69/EEC part B7; 6-weeks; 0, 200, 1000, 5000,10.000 ppm;	NOAEL: 196 mg/ kg bw/day = 181 (male) mg/kg bwt/day and 212 (female) mg/kg bwt/day	3940-91-0176-TX-003
Rat (males/ females)	Oral subacute	96.3	Guidelines 92/ 69/EEC part B7; 4-weeks; 0, 100, 1000, 5000, 10000, 20000 ppm;	NOAEL = 7.5 mg/kg bw/ day or 88 mg/kg bw/ day	87-1110
Rat (males/ females)	Oral Subchronic	96.3	Guideline US EPA FIFRA Pesticide assessment No. 82-1which is comparable to 87/302/ EEC part B; 13-weeks; 0, 40, 200, 1000, 5000 ppm;	NOAEL = 11.7 mg/kg bw/day o 61.5 mg/kg bw day	87-0112
Dog (males/ females)	Oral Subchronic	97.3	Guideline US EPA FIFRA Pesticide assessment No 82-1, which is comparable to 87/302/ EEC part B; 13-weeks; 0, 2, 10, 50, 250 (males) mg/kg bwt/day and 0, 2, 10, 50 100 (females) mg/kg bw/day;	NOAEL = 2 (m) or 10 (f) mg/kg bw/day	91-0056
Rabbit (males/ females)	Dermal	97.1	Guideline US EPA FIFRA Pesticide Assessment No 82-2; 21 day; 0, 125, 250, 500, 750, 1000 mg/kg/day;	NOAEL = 1000 mg/kg bw/day	5513-92-0456-TX-002
Rabbit (males / females)	Dermal	97.3	Guideline US EPA FIFRA Pesticide Assessment No. 82-2, which is comparable to 92/69/ EEC Part B9; 21 day; 0, 250, 500, 1000 mg/kg/day;	NOAEL = 1000 mg/kg bwt/day	5675-93-0077-TX-002
Rat, Fischer rats (344/DuCrj)	Chronic and oncogenic Fisher rat	97.3	Guideline 83-5, 87/302/EEC Part B , US EPA FIFRA; 24-Month; 40, 400, 2000 ppm or 40, 400 and 4000;	NOEL = 1.3 mg/kg bwt/day	91-0054

[2] Note: Purity is the content of pure active ingredient in the technical material, expressed as a percentage.

Species	Test	Purity % Note[32]	Duration and conditions	Result	Reference
Mice (male/ female)	Oncogenicity	97.3	US EPA FIFRA Pesticide Assessment Guidelines No. 83-2, is comparable to 87/302/EEC Part B; 18 month; 0, 500, 3500, 7000 ppm	NOEL = 80 mg/kg bwt/day (m: 70.4, f: 88.5)	3941-92-0020-TX-003
Dog (male/ female)	Oral Chronic	97.3	US EPA FIFRA Pesticide Assessment Guidelines No.82-1, comparable to 87/302/EEC Part B; 52 weeks; 0, 0.4, 2.0, 10.0, 50.0 and 0, 2.0, 10.0, 50.0 mg/kg bw	NOEL= 2 mg/kg bwt/day	91-0057
Rat (male/ female)	Reproductive	97.3	US EPA FIFRA Pesticide Assessment Guidelines No. 83-4 comparable to 87/302/EEC Part B; 12 months ; 0, 200, 2000, 10,000 ppm	NOEL= 653 mg/kg bwt/day Pup body bwt - NOEL= 240 mg/kg wt/day	5330-92-0223-TX-004
Rat (male/ female)	Develop-mental: Wistar - Imamichi	96.3	US EPA FIFRA Pesticide Assessment Guidelines No. 83-3 comparable to 92/69/EEC Part B; 21 days; 0, 100, 300, 1000 mg/kg bw/day;	NOEL= 100 mg/kg bwt/day	208-B
Rat (male/ female)	Developmental	97.3	US EPA FIFRA Pesticide Assessment Guidelines No. 83-3 comparable to 92/69/EEC Part B; 20 days; 0, 100, 300, 1000 mg/kg bw/day;	NOEL= 100 mg/kg bwt/day	6188-94-0195-TX-003
Rabbits (male/ female)	Developmental	96.3	Guidelines of MAFF in Japan (59 Nohsan 4200), EPA in the USA; OECD. These guidelines are comparable to 92/69/EEC Part B; 28 days; 0, 50, 150, 450 mg/kg bw/day;	NOEL 150 mg/kg bwt/day	209-B

Table 5. Mutagenicity profile of technical flazasulfuron based on *in vitro* and i*n vivo* tests

Species	Test	Purity % Note[42]	Duration and conditions	Result	Reference
Bacteria *(Salmonella typhimurium and Escherichia coli)*	reverse gene mutation, *in vitro*	96.3	Agricultural Chemical Laws and Regulations Japan (II),Testing Guidelines for Toxicology, Directive 92/69/EEC Method B14, US EPA Pesticide Assessment Guidelines Subdivision F Hazard Evaluation; 48 hours; 100, 200, 500, 1000, 2000, 5000 μg/plate (± S9);	No genotoxic potential	87-0122
Bacillus subtilis rec-assay	DNA Repair Test (Rec-Assay)	96.3	Agricultural Chemical Laws and Regulations Japan (II),Testing Guidelines for Toxicology, US EPA Pesticide Assessment Guidelines Subdivision F Hazard Evaluation; duration: overnight; 0, 20, 50, 100, 200, 500, 1000 µg/plate;	No genotoxic potential	87-0122
Chinese hamster lung (CHL) cells	*in vitro* cytogenetics test	96.3	92/69/EEC Part B10; 24 or 48 hours; 3.3 x 10^{-4}, 1.7 x 10^{-4}, 8.3 x 10^{-5}, 4.1 x 10^{-5}, 2.1 x 10^{-5} M (without metabolic activation), 1.0 x 10^{-2}, 5.0 x 10^{-3}, 2.5 x 10^{-3}, 1.3 x 10^{-3}, 6.3 x 10^{-4} M (with metabolic activation);	No clastogenic potential	87-0123
L5178Y $TK^{+/-}$ mouse lymphoma cells	*In vitro* mammalian cell forward gene mutation assay	97.1	Directive 87/302/EEC Part B and OECD Guideline 476,US EPA Pesticide Assessment Guidelines Subdivision F Hazard Evaluation; 48 hours; 20, 30, 40, 50, 60, 70, 80, 90, 100, 500 µg/mL;	No genotoxic potential	5542-93-0046-TX-003
ICR mice (male/ female)	Gene Mutations Chromosomal Aberration	97.1	Directive 92/69/EEC Method B12, OECD Guideline 474;US EPA Guideline; 72 hours; 0, 1250, 2500, 5000 mg/kg bw	No genotoxic potential	5542-93-0047-TX-003

[2] Note: Purity is the content of pure active ingredient in the technical material, expressed as a percentage.

Table 6. Ecotoxicology profile of technical flazasulfuron

Species	Test	Purity % Note[52]	Duration and conditions	Result	Reference
Bobwhite quail	Acute oral	96.3	Pesticide Assessment Guideline US EPA FIFRA, No. 71-1.; 14-days; 0, 500, 1000, 2000 mg/kg bw;	LC_{50} > 2000 mg/kg bw	16/881718
Mallard duck	Acute oral	97.2	Pesticide Assessment Guidelines US EPA FIFRA No. 71-1.; 14 days; 0, 292, 486, 810, 1350, 2250 mg/kg bwt;	LC_{50} > 2250 mg/kg bw	5462-92-0378-TX-003
Mallard duck	Dietary	97.2	ASTM standard E857-87, US EPA FIFRA Pesticide Assessment Guidelines,No.71-2 is comparable to OECD; 5 days; 0, 562, 1000, 1780, 3160, 5620 ppm;	LC_{50} > 5620 ppm	5463-92-0376-TX-003
Northern Bobwhite	Dietary	97.2	Guidelines: ASTM standard E857-87, US EPA FIFRA Pesticide Assessment, No.71-2 is comparable to OECD; 5 days; 0, 562, 1000, 1780, 3160, 5620 ppm;	LC_{50} > 5620 ppm	5463-92-0377-TX-003
Mallard duck (*Anas platyrhynchos*)	Reproductive	97.3	ASTM "Standard Practice for Conducting Reproductive Studies with Avian Species E1062-86, the US EPA FIFRA Pesticide Assessment, No. 71-4 and OECD Method 206; 21 weeks; 0, 100, 500, 1000 ppm;	1000 ppm	5589-93-0005-TX-003
Northern Bobwhite (*Colinus virginianus*)	reproductive	97.3	ASTM "Standard Practice for Conducting Reproductive Studies with Avian Species E1062-86, the US EPA FIFRA Pesticide Assessment, No. 71-4 and OECD Method 206; 21 weeks;0, 100, 500, 1000 ppm;	NOEL = 1000 ppm	5589-93-0006-TX-003
Rainbow trout	Acute toxicity	97.1	Pesticide Assessment Guideline US EPA FIFRA, No. 72-1, EPA Standard Evaluation Procedure, ASTM Standard E 729-88 Standard Practice for Conducting Acute Toxicity Tests with Fishes comparable to 92/69/EEC Part B; 96 hours; 8.1, 13, 20, 33,52 mg/L;	LC_{50} = 22 mg/L	5516-92-0461-TX-002

[2] Note: Purity is the content of pure active ingredient in the technical material, expressed as a percentage.

Species	Test	Purity % Note[52]	Duration and conditions	Result	Reference
Bluegill Sunfish	Acute toxicity	97.1	US EPA FIFRA Pesticide Assessment Guidelines No. 72-1, EPA Standard Evaluation Procedure, ASTM Standard E 729-88, Standard Practice for Conducting Acute Toxicity Tests with Fishes comparable to 92/69/EEC Part B; 96 hours; 15, 24, 38, 66, 98 mg/L;	LC_{50} > 98 mg/L	5516-92-0460-TX-002
Daphnia magna (water flea)	acute toxicity	97.1	US EPA FIFRA Pesticide Assessment Guidelines, ASTM Standart E729-88; 48 hours; 14, 24, 40, 66, 110 mg/L;	EC_{50} > 106 mg/L	5517-92-0459-TX-002
Pseudokirchneriella subcapitata	Acute toxicity Inhibition Test	95.7	OECD Guideline, Section 2, Test guideline 201, Directive 92/69 EEC; 72 hours; first test: 0.0097, 0.021, 0.047, 0.104, 0.228, 0.5 mg/L, second test: 0.0097, 0.021, 0.034, 0.047, 0.075, 0.104 mg/L;	NOEC = 0.034 mg/L 0,045 mg/L	398114
Anabaena flos-aquae (Cyanophyta)	Acute toxicity Inhibition Test	97.3	Guidelines Commission Directive 92/96/EEC, Annex Part C.C3, OECD No.201; 96 hours; 1.0, 3.2, 10, 32, 100 µg/L;	NOEC = 0.005 mg/L	628064
Lemna gibba G3	Growth inhibition	97.3	Guidelines US EPA Part 790 Section 797.1160; 7 days; 0.010, 0.032, 0.10, 0.32, 1.0 µg/L;	NOEC = 0.00002 mg/L EC_{50} = 0.00004 mg/L	628075
Rainbow Trout	Chronic toxicity	95.1	Guidelines OECD, Nr. 204; 21-Day; 0.078, 0.313. 1.25, 5.0, 20 mg/L;	NOEC = 5.0 mg/L	600862
Daphnia magna	reproductive		Guidelines OECD 202 Part II; 23 days; 0.39, 1.56, 6.25, 25.0, 100 mg/L; purity 95.7 %	NOEC = 6.25 mg/L	600873
Honey bees	acute, contact and oral	96.3	EPPO Guideline 170, UK Pesticide Safety Precautions scheme: Working Document D3; 48 hours; 5 doses from 0.01 to 100 µg/bee, final test: 0.100 µg/bee;	LC_{50} > 100 µg /bee LD_{50} > 100 µg/bee	17/881430

Species	Test	Purity % Note[52]	Duration and conditions	Result	Reference
Typhlodromus pyri	Laboratory test	95.7	The test method followed the procedure according to "Open test design as a standard laboratory test for predatory mites, based on the Overmeer testing method (Guideline for testing the effects of pesticides on beneficial Overmeer W.P.J; 14 days; 0.02 kg a.s/ha (40% of the maximum application rate)	Effect 11%, beneficial capacity	1202063
Poecilus cupreous	Laboratory test	95.7	BBA, Guideline part VI, Nr. 23.-2.1.8 and IOBC/WPRS Bulletin 1992/XV/3: 103-109; 14 days; 0.05 kg a.s./ha;	No effect (mortality, behavioural and consumption)	1201006
Pardosa sp	Laboratory test	95.7	BBA, Guideline testing pesticides for registration: Vorlaeufige Richtlinie fuer die Prufung von Pflanzenschutzmitteln im Zulassungsverfahren; 14 days; 0.05 kg a.s./ha;	No effect (mortality, behavioural and consumption)	1203066
Earthworm *Eisenia foetida*	acute toxicity	96.3	Guidelines UK Pesticides Safety Precautions Scheme (PSPS) Appendix D, Wildlife and Environmental Data Requirements: Working Document D6, Laboratory and Field Effects on Soil Macro-Organisms, S4; 14 days; 0, 0.16, 0.47, 1.57, 4.72,15.75 ppm a.s. (concentration in soil);	LC_{50} = 15.75 ppm dry mg/kg soil	14/88903
Soil micro-organismes – soil respiration	Soil Respiration and nitrification	95.1	Guidelines: BBA (Federal Biological Institute for Agriculture and Forestry), Part VI, 1-1, Effects on the activity of soil microflora; 0 to 3 hours, 14 and 28 days, 2 additional sampling of 56 and 98 days; 0.05 kg a.s./ha, 0.5 kg a.s./ha	no relevant effect	397956

HAZARD SUMMARY

Flazasulfuron has not been evaluated by the WHO IPCS or by the FAO/WHO JMPR.
There is no IPCS hazard classification for flazasulfuron.
In Europe the harmonised classification according to Annex VI of the CLP regulation is GHS09 (Warning); hazard classes: Aquatic acute 1 and Aquatic Chronic 1 with according hazard statements H400 and H410.

ANNEX 2

REFERENCES

Study number	Author(s)	year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
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