FAO SPECIFICATIONS AND EVALUATIONS

FOR AGRICULTURAL PESTICIDES

CHLORSULFURON

1-(2-chlorophenylsulfonyl)-3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)urea

2003

FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

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FAO specifications are developed with the basic objective of promoting, as far as practicable, the manufacture, distribution and use of pesticides that meet basic quality requirements.

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.

Furthermore, pesticides which are manufactured to comply with these specifications are not exempted from any safety regulation or other legal or administrative provision applicable to their manufacture, sale, transportation, storage, handling, preparation and/or use.

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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 has followed the **New Procedure**, first 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 Paper No. 149) and, subsequently, in the 1st edition of the "Manual for Development and Use of FAO and WHO Specifications for Pesticides" (FAO Plant Production and Protection Paper No. 173, 2002). 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).

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** was changed. Every specification now consists 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 pesticide, in accordance with chapters 4 to 9 of the 1st edition of the "FAO/WHO Manual on Pesticide Specifications."

Part Two: The Evaluation Report(s) of the pesticide, reflecting the evaluation of the data package carried out by FAO and the JMPS. The data are provided by the manufacturer(s) according to the requirements of chapter 3 of the "FAO/WHO Manual on Pesticide Specifications" 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 developed 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 those which formed the basis of the reference specification.

* Footnote: The publications are available on Internet under (http://www.fao.org/AG/AGP/AGPP/Pesticid/) or as hardcopy from the Plant Protection Information Officer.

PART ONE

SPECIFICATIONS

CHLORSULFURON

CHLORSULFURON INFORMATION
CHLORSULFURON TECHNICAL MATERIAL
CHLORSULFURON WETTABLE POWDERS
CHLORSULFURON WATER DISPERSIBLE GRANULES

Chlorsulfuron

INFORMATION

Common name:
chlorsulfuron (E-ISO, (m)F-ISO, ANSI, WSSA)

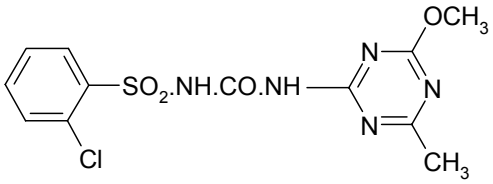
Synonyms:
none

Chemical names

IUPAC: 1-(2-chlorophenylsulfonyl)-3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl) urea

CA: 2-chloro-*N*-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl] benzenesulfonamide

Structural formula:



Molecular formula:
$C_{12}H_{12}ClN_5O_4S$

Relative molecular mass:
357.8

CAS Registry number:
64902-72-3

CIPAC number:
391

Identity tests:
HPLC-UV retention time, IR spectrum

CHLORSULFURON TECHNICAL MATERIAL

FAO Specification 391/TC (2003)

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 (391/2003). It should be applicable to relevant products of the company 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 (391/2003), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of chlorsulfuron, together with related manufacturing impurities, and shall be a light grey, homogeneous, fine crystalline solid, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (391/TC/M/2, CIPAC Handbook H, p. 90, 1998)

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 **Chlorsulfuron content** (391/TC/M/3, CIPAC Handbook H, p. 90, 1998)

The chlorsulfuron content shall be declared (not less than 950 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

CHLORSULFURON WETTABLE POWDER

FAO Specification 391/WP (2003)

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 (391/2003). It should be applicable to relevant products of the company 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 (391/2003), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of a homogeneous mixture of technical chlorsulfuron, complying with the requirements of FAO specification 391/TC (2003), together with filler(s) and any other necessary formulants. It shall be in the form of a fine powder, free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 **Identity tests** (391/WP/M/2, CIPAC Handbook K, p. 24, 2003)

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 **Chlorsulfuron content** (391/WP/M/3, CIPAC Handbook K, p. 24, 2003)

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

Declared content in g/kg	Permitted tolerance
above 500	± 25 g/kg

3 Physical properties

3.1 **Wet sieve test** (MT 185, CIPAC Handbook K, p.149, 2003)

Maximum: 2% retained on a 75 μm test sieve.

3.2 **Suspensibility** (MT 15.1, CIPAC Handbook F, p. 45, 1995; MT 177, CIPAC Handbook F, p. 445, 1995; MT 184, CIPAC Handbook K, p.142, 2003) (Notes 1 & 2)

A minimum of 60% of the chlorsulfuron content found under 2.2 shall be in suspension after 30 min. in CIPAC Standard Water D at 30 ± 2°C (Note 3).

3.3 **Persistent foam** (MT 47.2, CIPAC Handbook F, p. 152, 1995) (Note 4)

Maximum: 60 ml after 1 minute.

3.4 **Wettability** (MT 53.3, CIPAC Handbook F, p. 164, 1995) (Note 5)

The formulation shall be completely wetted in 1 minute without swirling.

4 **Storage stability**

4.1 **Stability at_elevated temperature** (MT 46.3, CIPAC Handbook J, p. 128, 2000)

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 (3.1)
- suspensibility (3.2);
- wettability (3.4).

Note 1 The formulation should be tested at the highest and lowest use rates recommended by the supplier, provided this does not exceed the conditions given in methods MT15.1 or MT177 or MT 184.

Note 2 This test will normally only be carried out after the heat stability test 5.1.

Note 3 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, simpler methods such as gravimetric and solvent extraction determination may be used on a routine basis, provided that these methods have been shown to give equal results to those of the chemical assay. 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 of use recommended by the supplier.

Note 5 The product should be tested at 0.5 g. Although this amount of test substance is well below the 5.0 gram sample size required by MT 53.3, it is still far in excess of the maximum concentration recommended for use and does constitute sufficient quantity to enable an accurate visual determination of wettability.

Note 6 Samples of the formulation taken before and after the storage stability test should be analyzed concurrently after the test in order to reduce the analytical error.

CHLORSULFURON WATER DISPERSIBLE GRANULES

FAO Specification 391/WG (2003)

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 (391/2003). It should be applicable to relevant products of the company 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 (391/2003), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of a homogeneous mixture of technical chlorsulfuron, complying with the requirements of FAO specification 391/TC(2003), together with carriers and any other necessary formulants. It shall be in the form of spherical 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.

Where the material is packaged in sealed water-soluble bags, the material shall consist of a defined quantity of chlorsulfuron water dispersible granules complying with the requirements of FAO specification 391/2003, contained in a sealed water-soluble bag

2 Active Ingredient

2.1 **Identity tests** (391/WG/M/2, CIPAC Handbook H, p. 90, 1998)

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 **Chlorsulfuron content** (391/WG/M/3, CIPAC Handbook H, p. 92, 1998)

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

Declared content in g/kg	Permitted tolerance
above 500	± 25 g/kg

3 Physical properties

3.1 **Wettability** (MT 53.3, CIPAC Handbook F, p. 164, 1995)

The formulation shall be completely wetted in 10 sec., without swirling.

3.2 **Wet sieve test** (MT 185, CIPAC Handbook K, p.149, 2003)

Maximum: 2% retained on a 75 µm test sieve.

3.3 **Degree of dispersion** (MT 174, CIPAC Handbook F, p. 435, 1995)

Dispersibility: minimum: 80% after 1 minute of stirring.

3.4 **Suspensibility** (MT 168, CIPAC Handbook F, p. 417, 1995; MT 184, CIPAC Handbook K, p.142, 2003) (Notes 1 & 2)

A minimum of 60% of the chlorsulfuron content shall be in suspension after 30 min. in CIPAC standard water D at 30 ± 2ºC.

3.5 **Persistent foam** (MT 47.2, CIPAC Handbook F, p. 152, 1995) (Note 3)

Maximum: 60 ml after 1 min.

3.6 **Dustiness** (MT 171, CIPAC Handbook F, p. 425, 1995) (Note 4)

Essentially non-dusty.

3.7 **Flowability** (MT 172, CIPAC Handbook F, p. 430, 1995)

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

4 Storage stability

4.1 **Stability at elevated temperature** (MT 46.3, CIPAC Handbook J, p. 128, 2000)

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 5), 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).

In the case of water-soluble bag packaging, the package should be enclosed in a watertight sachet, box or other container at 45 ± 2°C for 8 weeks. The determined average active ingredient content must not be lower than 95% relative to the determined average content found before storage (Note 5), and the formulation shall continue to comply with the clauses for:

- degree of dispersion (3.3);
- suspensibility (3.4);
- dustiness (3.6);
- dissolution of the bag (5.1)
- persistent foam (5.3).

5 Material Packaged in a sealed water soluble bag (Notes 6, 7 & 8)

5.1 **Dissolution of the bag** (MT176, CIPAC Handbook F, p. 440, 1995)

The dissolution of the bag shall be tested on a sample of the emptied and cleaned bag taken according to the procedure described in Note 7, together with an appropriate proportion of the WG.

Flow time of suspension: maximum 30 sec.

5.2 **Suspensibility** (MT 168, CIPAC Handbook F, p. 417, 1995; MT 184, CIPAC Handbook K, p.142, 2003) (Notes 1, 2 & 8)

The suspensibility shall be tested on a suspension containing the WG and the bag material in the actual ratio of application, prepared according to the procedure described in Note 8.

A minimum of 60% shall be in suspension after 30 min in CIPAC Standard Water D at 30 ± 2ºC.

5.3 **Persistent foam** (MT 47.2, CIPAC Handbook F, p. 152, 1995)(Note 3)

The persistent foam shall be tested on a suspension containing the WG and the bag in the actual ratio of application, prepared according to the procedure described in Note 8.

Maximum: 60 ml after 1 min.

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Note 1 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 method MT 168 and MT 184.

Note 2 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method, MT 168, may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the "referee method".

Note 3 The mass of sample to be used in the test should be specified at the highest rate recommended by the supplier.

Note 4 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, usually shows good correlation with the gravimetric method 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 5 Analysis of the formulation, before and after the storage stability test, should be carried out concurrently (i.e. after storage) to reduce analytical error.

Note 6 Sub-sampling
Lay the bag on a bench and carefully open one side of the bag with a cutter, taking care not to damage the seals.

Transfer the contents of the bag into a suitable flask. This material shall be used to carry out the tests for:

- active ingredient identity (2.1),
- active ingredient content (2.2),
- wettability (3.1),
- wet sieve test (3.2),
- degree of dispersion (3.3),
- dissolution of the bag (5.1),
- suspensibility (5.2),
- persistent foam (5.3).

The bag is then opened on three sides, completely cleaned from adhering powder by brushing or suction and weighed to the nearest 0.01 g. It shall be used to carry out the dissolution test (5.1). Aliquots of an aqueous solution of the bag material shall be used in the suspensibility (5.2) and persistent foam (5.3) tests.

In the case of delay of the above tests, the bag shall be stored in a watertight container (glass bottle or equivalent) to avoid any change in its properties.

Note 7 The sampling of the bag for the dissolution test should be as follows:

Lay the empty cleaned bag in its original configuration (double layer). Delineate and then cut up a test sample including part of the upper seal (5 cm) and symmetrically, including the vertical seal (10cm).

If the size of the bag is less than this dimension, use the whole bag.

Carry out the dissolution test immediately to avoid any modification of the sample.

Note 8 The procedure for adding the bag material to the solution for the rate of dissolution, suspensibility and the persistent foam tests should be as follows:

Prepare a stock solution of the bag material (1 mg/ml) by weighing approximately a 100 mg sample (n mg) of the bag (excluding sealed parts) to the nearest mg. Dissolve this sample by stirring in the standard water used for tests, to give a final volume of n ml. Store the stock solution in a stoppered bottle before use.

Calculate the volume (V ml) of the stock solution of the bag to be added to the test suspension of the water soluble powder according to the following equation:

$$\mathbf{V(ml) = X \times \frac{1000B}{W}}$$

where: B (g) = weight of the emptied and cleaned bag;
W (g) = nominal weight of the WG contained in the bag;
X (g) = weight of the WG sample used in the test.

PART TWO

EVALUATION REPORTS

CHLORSULFURON

2003 FAO/WHO evaluation report based on submission of data from E.I. du Pont de Nemours and Company (TC, WG, WP)

FAO/WHO EVALUATION REPORT 391/2003

CHLORSULFURON

Explanation

The data for chlorsulfuron were submitted in support of review of existing FAO specifications, developed in 1997 and 2000, according to the previous procedure (FAO, 2000).

A complete dossier on chlorsulfuron will be submitted to the EU, for inclusion of the active ingredient in Annex I of Directive 91/414/EEC, in November 2004, with Greece as the rapporteur member state. At the time of evaluation, re-registration of chlorsulfuron was in progress in the USA, with completion expected in 2003.

Chlorsulfuron has not been evaluated by the FAO/WHO JMPR or WHO/PCS.

The draft FAO specifications and the supporting data (some of which related to two sources of the active ingredient: Shanghai, PRC & Manati, Puerto Rico) were provided by E. I. du Pont de Nemours and Company, in September 2002.

Uses

Chlorsulfuron is a herbicide that acts by inhibiting the formation of acetolactate synthase (ALS) in susceptible plants. It is used in cereal crops for the control of broadleaf and grass weeds.

Identity

Common name:

chlorsulfuron (E-ISO, (m)F-ISO, ANSI, WSSA)

Synonyms:

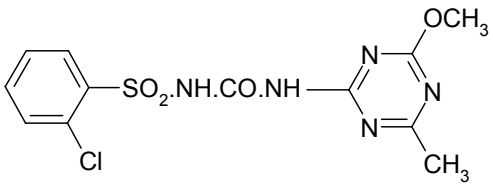
none

Chemical names

IUPAC: 1-(2-chlorophenylsulfonyl)-3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl) urea

CA: 2-chloro-*N*-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl] benzenesulfonamide

Structural formula:



Molecular formula:

$C_{12}H_{12}ClN_5O_4S$

Relative molecular mass:

357.8

CAS Registry number:

64902-72-3

CIPAC number:

391

Identity tests:

HPLC-UV retention time, IR spectrum

Physical and chemical properties of chlorsulfuron

Table 1. Physico-chemical properties of pure chlorsulfuron.

Parameter	Value(s) and conditions	Purity %	Method reference
Vapour pressure	3.0×10^{-9} Pa at 25°C (extrapolated)	~95	Knudsen gas effusion, in accordance with: EEC Method A.3., USEPA 63-9 USEPA 830.7950
Melting point, boiling point and/or temperature of decomposition	Melting point: 170-173°C Boiling point: NA Decomposition temperature: approx. 150°C. Decomposition was observed throughout the melt.	98.0	OECD 102
Solubility in water	0.59 g/l at 25°C at pH 5.0 31.8 g/l at 25°C at pH 7.0	93.1	Shake flask HPLC, in accordance with: EEC Method A.6. USEPA 63-8
Octanol/water partition coefficient	log P_{OW} = 0.32-0.34 at 25°C at pH 5.0 log P_{OW} = -1.02-0.96 at 25°C at pH 7.0 log P_{OW} = -1.41 at 25°C at pH 9.0	96.0	USEPA 63-11, in accordance with: EEC Method A.8. USEPA 830.7550
Hydrolysis characteristics	Half-life = 23 days at 25°C at pH 5.0 Half-life = stable, (>31 days) at 25°C at pH 7.0 Half-life = stable, (>31 days) at 25°C at pH 9.0	~95	EPA 161-1 (USEPA, 1982a)
Photolysis characteristics	Photolysis half-life 17-19 days in sterile buffer at pH 5 and 25ºC. No significant (>5%) photolysis observed at pH 7 and pH 9	~95	EPA 161-2 (USEPA, 1982b)
Dissociation characteristics	pKa = 3.4	99.93	UV spectrophotometric method, in accordance with: OECD 112 USEPA 63-10 USEPA 830.7370

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

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 10 batch analysis data	Confidential information supplied and held on file by FAO. Mass balances were 99.0–100.7%.
Declared minimum chlorsulfuron content	950 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.
Melting or boiling temperature range of the TC	170-173°C, decomposition starts around 150°C.

Toxicological summaries

Notes.

(i) The proposer confirmed that the toxicological and ecotoxicological data included in the summary below were derived from chlorsulfuron 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 chlorsulfuron technical material, based on acute toxicity, irritation and sensitization.

Species	Test	Duration and conditions or guideline adopted	Result
Rat, ChR-CD, (M/F)	Oral	14-day recovery period EEC B.1, OECD 401, USEPA 81-1, USEPA 870.1100, MAFF Japan 1985 Chlorsulfuron TC (~95%)	LD_{50} = 5545 mg/kg bw (males) LD_{50} = 6293 mg/kg bw (females)
New Zealand White rabbit, (M/F)	Dermal	24-hour exposure period EEC Method B.3., OECD 402, USEPA 81-2, USEPA 870.1200, MAFF Japan 1985 Chlorsulfuron TC (~95%)	LD_{50} = >3400 mg/kg bw for both male and female rabbits. No clinical signs or deaths were observed.
Rat, ChR-CD, (M/F)	Inhalation	Exposed 4 hours EEC Method B.2., OECD 403, USEPA 81-3, USEPA 870.1300, MAFF Japan 1985 Chlorsulfuron TC (~95%)	$LC_{50} \geq$ 5.9 mg/l No mortalities were observed. No unusual clinical signs were observed during the exposure.
New Zealand White rabbit, HM:(NZW)fBR, (M)	Skin irritation [1/]	4-hour exposure period. EEC Method B.4., OECD 404,USEPA 870.2500, MAFF Japan 1985 Chlorsulfuron TC (97.15%)	Dermal non-irritant (according to EEC Directive 93/21). No oedema, and only infrequent minimal erythema (at 24 h) observed at 24, 48, or 72 hours.
New Zealand White rabbit (M/F)	Eye irritation	EEC Method B.5, OECD 405, USEPA 81-4, USEPA 870.2400, MAFF Japan 1985 Chlorsulfuron TC (96.2%)	Non-Irritant, according to EEC Directive 93/21. The treated eyes of all rabbits were normal 72 hours after treatment.

Species	Test	Duration and conditions or guideline adopted	Result
Guinea pig, albino (M)	Skin sensitization	Test conducted prior to issuance of formal test guidelines. Ten animals induced by four weekly intradermal injections of 1% chlorsulfuron (w/v) in dimethylphthalate, followed after a 2-week rest, then topical challenge with 3% or 30% (w/v) chlorsulfuron in propylene glycol. Negative controls included. No positive controls. Chlorsulfuron TC (~95.0%)	Non-sensitizer. Produced no irritation on shaved intact skin. No sensitization was observed at challenge.

[1/] New data, not yet evaluated by national registration authorities.

Table 4. Toxicology profile of chlorsulfuron technical material, based on repeated administration (sub-acute to chronic).

Species	Test	Duration and conditions or guideline adopted	Result
Rat, (ChR-CD®) Charles River, (M/F)	Oral 90-day study	Directive 87/302/EEC, OECD 408, USEPA 82-1, USEPA 870.3100, MAFF Japan 1985 Chlorsulfuron TC (~95.0%)	NOAEL = 2500 ppm 137 mg/kg bw/day)
Mouse, (ChR-CD®-1), (M/F)	Oral 90-day study	Directive 87/302/EEC, OECD 408, USEPA 82-1, USEPA 870.3100, MAFF Japan 1985 Chlorsulfuron TC (~95.0%)	NOAEL = 2,500 ppm (783 mg/kg bw/day)
Beagle dog (M/F)	Oral 1-year study	Directive 87/302/EEC part B; OECD 408 Chlorsulfuron TC (97.5%)	NOAEL = 2000 ppm (61 mg/kg bw/day)
Rat, (ChR-CD®) Charles River, (M/F)	2-year feeding and 3-generation reproduction	Directive 87/302/EEC, OECD 453, USEPA 83-5, USEPA 870.4300, MAFF Japan 1985 Chlorsulfuron TC (95%, 91.9%)	Overall NOAEL = 100 ppm (4 mg/kg bw/day) Reproduction NOAEL = 500 ppm (20 mg/kg bw/day). No carcinogenicity at any level in 2-year study. Not a reproductive toxin.
Mouse, (ChR-CD®-1), (M/F)	2-year feeding study	Directive 87/302/EEC, OECD 451, USEPA 83-2, USEPA 870.4200, MAFF Japan 1985 Chlorsulfuron TC (95%, 91.9%)	NOAEL = 500 ppm (72 mg/kg bw/day). Not carcinogenic at any level.
Rat, (Crl:CD®BR), (F)	Teratogenicity	Directive 87/302/EEC, OECD 414, USEPA 83-3, USEPA 870.3700, MAFF Japan 1985 Chlorsulfuron TC (98.2%)	NOAEL = 165 mg/kg bw/d (dam) NOAEL = 500 mg/kg bw/d (pups). Not a developmental toxin and not selectively toxic to the conceptus.

Species	Test	Duration and conditions or guideline adopted	Result
New Zealand White rabbit (F)	Teratogenicity	Directive 87/302/EEC, OECD 414, USEPA 83-3, USEPA 870.3700, MAFF Japan 1985 Chlorsulfuron TC (98.2%)	NOAEL = 200 mg/kg bw/d (dam) NOAEL = 1000 mg/kg bw/d (pups). Not a developmental toxin and not selectively toxic to the conceptus.

Table 5. Mutagenicity profile of chlorsulfuron technical material, based on *in vitro* and *in vivo* tests.

Species	Test	Conditions	Result
Salmonella typhimurium	*In vitro* bacterial gene mutation assay	Absence and presence of an exogenous metabolic activation system. EEC Method B.13., EEC Method B.14, OECD 471, OECD 472, USEPA 84-2, USEPA 870.5265, MAFF Japan 1985 Chlorsulfuron TC (99.3%)	Not mutagenic in bacteria, Negative for mutagenic activity.
Chinese hamster ovary (CHO) cells	*In vitro* cytogenetic assay (chromosome aberration)	Absence and presence of an exogenous metabolic activation system. EEC Method B.10., OECD 473, USEPA 84-2, USEPA 870.5375 Chlorsulfuron TC (95%)	Negative for chromosomal aberration activity.
Rat primary hepatocytes	*In vitro* unscheduled DNA synthesis (UDS) assay	87/302/EEC; OECD 482; USEPA 84-2; USEPA 870.5550, MAFF Japan 1985 Chlorsulfuron TC (98.2%)	Negative for UDS.
Chinese hamster ovary (CHO) cells	*In vitro* assay for mutagenicity (HGPRT)	87/302/EEC, OECD 476, USEPA 84-2, USEPA 870.5300 Chlorsulfuron TC (95%)	Not mutagenic in mammalian cells.
Rat (ChR-CD®) Charles River	*In vivo* dominant lethal assay	87/302/EEC Chlorsulfuron TC (~95%)	Not mutagenic in germ cells.

Table 6. Ecotoxicology profile of chlorsulfuron technical material.

Species	Test	Duration and conditions	Result
Daphnia magna (water flea)	48-hour acute toxicity [1/]	U.S. EPA Pesticide Assessment Guideline; FIFRA 72-2 (a); OECD Guideline for Testing Chemicals, No. 202 (adopted April 1984); EEC 92/69 Annex V, Method C.2 (1992) USEPA 850.1010 Chlorsulfuron TC (97.18%)	EC_{50} = >112 mg/l
Daphnia magna (water flea)	21-day semi-static chronic toxicity	U.S. EPA Pesticide Assessment Guideline; Subdivision E, 72-4; OECD Guideline for Testing Chemicals, No. 202 (1984) USEPA 850.1300 Chlorsulfuron TC (95.4%)	NOEC = 12 mg/l NOEL = 20 mg/l, based on reproduction effects.

Species	Test	Duration and conditions	Result
Selenastrum capricornutum (green alga)	120-hour effect on growth and growth rate	EEC Method C.3., USEPA 122-2, USEPA 123-2, USEPA 850.5400 Chlorsulfuron TC (98.2%)	EC_{50} = 50 μg/l NOEL = 10 μg/l
Anabaena flos-aquae (blue-green alga)	120-hour effect on growth and growth rate [1/]	EEC Method C.3., OECD 201, USEPA 122-2, USEPA 123-2, USEPA 850.5400 Chlorsulfuron TC (97.9%)	EC_{50} = 0.609 mg/l NOEC = 0.236 mg/l calculated using the area under the growth curve.
Lemna gibba G3 (aquatic plant)	14-day influence on growth and reproduction [1/]	USEPA 122-2 & 123-2 ASTM E1415-91 Chlorsulfuron TC (97.8%)	EC_{50} = 0.42 μg/l (number of normal fronds) EC_{50} = 0.35 μg/l (biomass) NOEC = 0.24 μg/l (number of normal fronds or the biomass)
Apis mellifera (honey bee)	48-hour acute oral and contact toxicity [1/]	OECD 213 & 214, EPPO Guideline 170, USEPA 141-1 Chlorsulfuron TC (97.2%)	Contact: LD_{50} = >100 μg a.s./bee Oral: LD_{50} = >130 μg a.s./bee
Colinus virginianus (Bobwhite quail)	Acute oral toxicity	SETAC, OECD Draft Guidelines, USEPA 71-1, USEPA 850.2100 Chlorsulfuron Technical (~95%)	LD_{50} = >5000 mg/kg bw in both male and female
Colinus virginianus (bobwhite quail)	8-day acute dietary study	OECD 205, USEPA 71-2, USEPA 850.2200 Chlorsulfuron TC (~95%)	LC_{50} = >5620 mg/kg feed
Anas platyrhynchos (mallard duck)	Acute oral toxicity	SETAC, OECD Draft Guidelines, USEPA 71-1, USEPA 850.2100 Chlorsulfuron TC (~95%)	LD_{50} = >5000 mg/kg (M/F)
Anas platyrhynchos (mallard duck)	8-day acute dietary study	OECD 205, USEPA 71-2, USEPA 850.2200 Chlorsulfuron TC (~95%)	LC_{50} = >5000 mg/kg feed
Colinus virginianus (bobwhite quail)	22-week sub-chronic toxicity and reproduction	OECD 206, USEPA 71-4, USEPA 850.2300 Chlorsulfuron TC (97.5%)	NOEC = 200 mg/kg feed, based upon possible body weight gain at 1000 mg/kg.
Anas platyrhynchos (mallard duck)	20-week sub-chronic toxicity and reproduction	OECD 206, USEPA 71-4, USEPA 850.2300 Chlorsulfuron TC (97.5%)	NOEC = 1000 mg/kg feed (highest rate tested)
Oncorhynchus mykiss (rainbow trout)	Acute 96-hour static toxicity [1/]	EEC Method C.1., OECD 203, USEPA 72-1 Chlorsulfuron TC (97.2%)	LC_{50} = >122 mg/l measured (limit)
Lepomis macrochirus (bluegill sunfish)	Acute 96-hour static toxicity [1/]	EEC Method C.1., OECD 203, USEPA 72-1, Chlorsulfuron TC (97.2%)	LC_{50} = >128 mg/l measured (limit)
Oncorhynchus mykiss (Rainbow trout)	77-day flow through trout reproduction	OECD 210, USEPA 72-4, USEPA 850.1400 Chlorsulfuron TC (>97.9%)	NOEC = 32 mg/l, measured

[1/] New data, not yet evaluated by national registration authorities.

Chlorsulfuron specifications were developed under the old procedure by FAO in 1995 (AGP:CP/371,2000) but this did not involve any formal evaluation of impurities, hazards and risks. Chlorsulfuron has not been evaluated by FAO/WHO JMPR. It

has been classified by IPCS as unlikely to present acute hazard in normal use (Category U) (IPCS, 2002).

Formulations

The main formulation types available are water dispersible granules (WG) and wettable powders (WP). These formulations are registered and sold in many countries throughout the world.

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests) has been validated and adopted by CIPAC (CIPAC, 1998). Chlorsulfuron is determined by reversed-phase HPLC, using UV detection at 254 nm and internal standardization with phenyl sulfone.

The analytical method for determination of impurities was based on reversed-phase HPLC, using UV detection at 230 nm and external standardization.

Test methods for the determination of physico-chemical properties of the technical active ingredient were OECD, CIPAC, EPA, EEC, 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 and WP formulations, comply with the requirements of the Manual (FAO/WHO, 2002).

Containers and packaging

There are no special container or packaging requirements.

Expression of the active ingredient

The active ingredient is expressed as chlorsulfuron (free acid).

Appraisal

Chlorsulfuron is a systemic sulfonylurea herbicide, for the pre- and post-emergence control of most broad-leaved weeds and some annual grasses in wheat, barley, oats, rye, triticale, flax and on non-crop land. Chlorsulfuron is selective, acting through foliar and root uptake. It acts by inhibiting biosynthesis of the essential amino acids valine and isoleucine and stops cell division by inhibition of the acetolactate synthase enzyme. The application rate of the substance is low, with typical application rates between 9 and 25 g ai/ha. The main formulation types available are water dispersible granules (WG) and wettable powders (WP).

The data submitted were in accordance with the requirements of the Manual (FAO/WHO 2002) and supported the draft specifications.

The data summary submitted by the proposer in support of the physico-chemical, toxicological and ecotoxicological properties were in agreement with those evaluated as part of the Hungarian registration of chlorsulfuron, except for study results that had not been previously reported to regulatory agencies and are considered new data (i.e. dermal irritation study on male New Zealand white rabbits [OECD 404]; water flea acute toxicity study [OECD 202]; blue-green alga toxicity study [OECD 201]; duckweed growth inhibition study [US EPA 122-2 & 3]; honey bee toxicity study [OECD 213 & 214]; bluegill sunfish acute toxicity study [OECD 203]; and rainbow trout acute 96-hour static toxicity study [OECD 203]). These studies were submitted to the EU in 2003 in support a new EU registration. The data that had not been previously evaluated were informally assessed by the WHO/PCS secretariat, which noted that the studies were performed using recommended methodologies and according to good laboratory practice and that accurate summaries of the study results were provided.

Pure chlorsulfuron is a white, odourless crystalline solid of low vapour pressure. It is acidic and, as may be expected, the water solubility is pH dependent with higher solubility at higher pH values (590 mg/l at pH 5 and 31800 mg/l at pH 7). Chlorsulfuron hydrolyzes moderately rapidly in aqueous solution at pH 5 but is stable at pH 7 and 9 at 25°C. Its photolysis characteristics are also pH dependent, being moderately degradable at pH 5 with a photolytic half-life of 19 days but stable to direct photolysis in sterile buffer solutions at pH 7 and 9. The very low octanol-water partition coefficient indicates a low potential for bioaccumulation. The technical material is not classified as having explosive, oxidizing or flammable properties.

Chlorsulfuron is manufactured by the proposer at two sites. The Meeting was provided with commercially confidential information on the manufacturing process and batch analysis data on all impurities present, at or above 1 g/kg. These data were identical to those submitted to for registration in Hungary. The meeting agreed that none of the manufacturing impurities considered were, on the basis of information currently available, of toxicological or environmental concern. Mass balances were 99.0-100.7% and the minimum purity of the technical material from the two production plants was 968.6 g/kg, according to the 10-batch data. The purity of the technical material used in the toxicological studies was 91.9-99.3%. The overall manufacturing process for chlorsulfuron had not changed with time and, on a qualitative basis, there had been no change in the impurity profile.

As chlorsulfuron TC is slightly hygroscopic, the water recorded in the impurity profile was probably present due to absorption from the air. Chlorsulfuron TC was shown to be very stable to hydrolysis under normal storage conditions and the meeting agreed that water should not be considered as a relevant impurity.

The meeting considered the unexpected presence of methanol in the impurity profile, as it is not used in the manufacture of chlorsulfuron. The proposer confirmed that no methanol had been detected in technical materials from the two production sites. The analytical method used to measure residual solvents in the technical material is used for both xylene and methanol and, by error, methanol was included in the impurity profile. The same error occurred in the information provided to regulatory agencies.

The toxicological studies demonstrate that chlorsulfuron is of low acute, sub-acute and chronic toxicity; is devoid of irritation and sensitization capacities; is not toxic to reproduction; and is not carcinogenic or mutagenic. Chlorsulfuron was rapidly metabolized and eliminated from mammalian systems. The active substance and its metabolites do not accumulate in tissues.

The ecotoxicological studies demonstrate that chlorsulfuron is of low acute, and intermediate long-term, toxicity to *Daphnia magna*; of low toxicity to fish and birds; but is very toxic to green algae, blue green algae and also to other aquatic plants (e.g. *Lemna*) and would therefore be classified as dangerous for the environment (R50, very toxic to aquatic environment).

Chlorsulfuron has not been evaluated by the FAO/WHO JMPR. Chlorsulfuron has been classified by IPCS as unlikely to present acute hazard in normal use (Category U). Based on acute toxicity, classification of chlorsulfuron according to the criteria specified in Directive 67/548/EEC is not required.

The HPLC methods for determination of chlorsulfuron in the TC, WG and WP are full CIPAC methods (391/TC/M/3, 391/WG/M/3, 391/WP/M/3). Test methods for determination of physico-chemical properties of the technical active ingredient and formulations were OECD and CIPAC, as indicated in the specifications.

Recommendations

The meeting recommended that the existing FAO specifications for chlorsulfuron (391/TC/S/F, 1997; 391/WG/S/F, 1997 and 391/WP/S/P, 2000) should be withdrawn and that the proposed specifications (as amended) (TC, WP, WG) should be adopted by FAO.

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