FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

NICOSULFURON

1-(4,6-dimethoxypyrimidin-2-yl)-3-(3-dimethylcarbamoyl-2-pyridylsulfonyl)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/ag/agp/agpp/pesticid/)

OR IN HARDCOPY FROM THE PLANT PROTECTION INFORMATION OFFICER.

PART ONE

SPECIFICATIONS

NICOSULFURON

PART ONE

NICOSULFURON

INFORMATION

ISO common name

Nicosulfuron (E-ISO, BSI, ANSI)

Synonyms

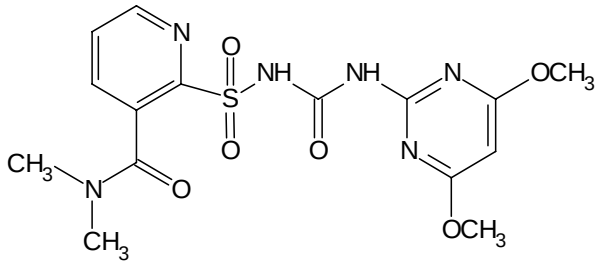
None

Chemical names

IUPAC 1-(4,6-dimethoxypyrimidin-2-yl)-3-(3-dimethylcarbamoyl-2-pyridylsulfonyl)urea

CA 2-[[[[(4,6-dimethoxyl-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]-*N*,*N*-dimethyl-3-pyridinecarboxamide

Structural formula



Empirical formula

$C_{15}H_{18}N_6O_6S$

Relative molecular mass

410.4

CAS Registry number

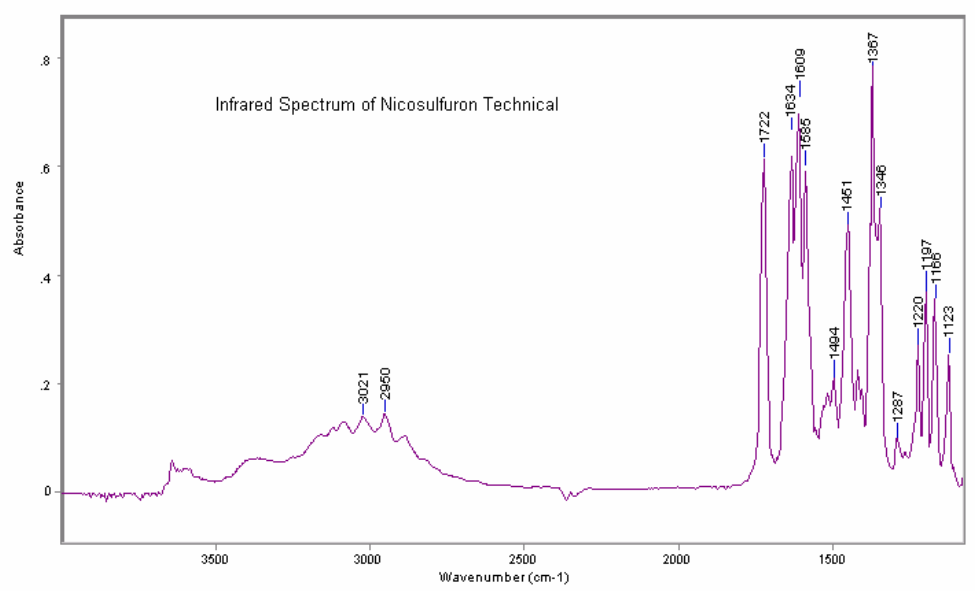
111991-09-4

CIPAC number

709

Identity tests

HPLC retention time; IR spectrum (page 4); UV spectrum (page 4)



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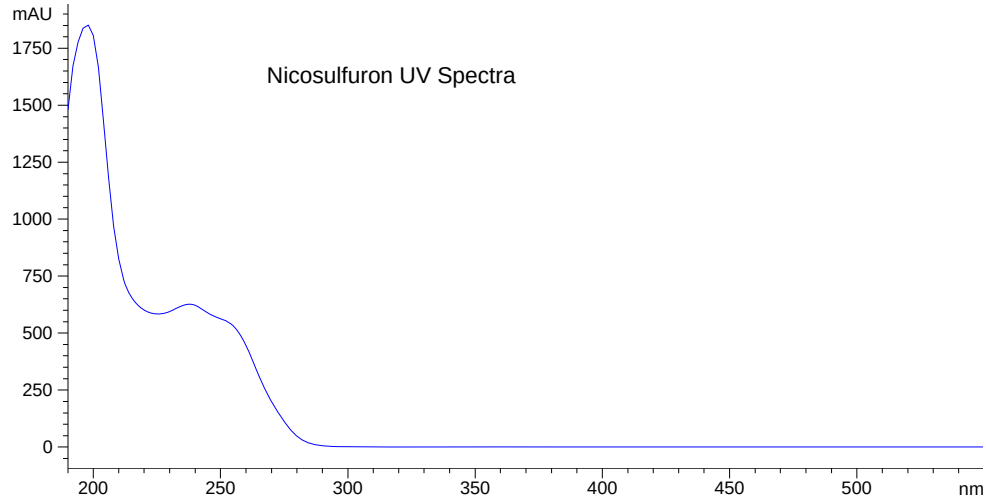


NICOSULFURON TECHNICAL MATERIAL

FAO specification 709/TC (May 2006*)

*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 (*709/2005*). 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 (*709/2005*) as PART TWO forms an integral part of this publication.*

1 Description

The material shall consist of nicosulfuron together with related manufacturing impurities and shall be a homogeneous white crystalline or powder solid, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity test**s (709/TC/M/2, CIPAC Handbook, 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 **Nicosulfuron content** (709/TC/M/3, CIPAC Handbook, Note 1)

The nicosulfuron content shall be declared (not less than 910 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

Note 1 Methods for the identification and determination of nicosulfuron content were adopted by CIPAC in 2005 but are not yet published in a Handbook. Prior to publication of the Handbook, copies of the methods may be obtained through the CIPAC website, http://www.cipac.org/prepubme.htm or from the CIPAC Secretary, Dr László Bura (mail to bura.laszlo@ntksz.ontsz.hu).

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: http://www.fao.org/ag/agp/agpp/pesticid/.

NICOSULFURON WATER DISPERSIBLE GRANULES

FAO specification 709/WG (May 2006*)

*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 (*709/2005*). 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 (*709/2005*) as PART TWO forms an integral part of this publication.*

1 Description

The material shall consist of a homogeneous mixture of technical nicosulfuron, complying with the requirements of the FAO specification 709/TC (May 2006), together with carriers and any other necessary formulants. It shall be in the form of 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** (709/WG/M/2, CIPAC Handbook, 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 **Nicosulfuron content** (709/WG/M/3, CIPAC Handbook, Note 1)

The nicosulfuron 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, g/kg	Tolerance
above 500	± 25 g/kg

3 Physical properties

3.1 **Wettability** (MT 53.3.1, CIPAC Handbook F, p.165, 1995)

The formulation shall be completely wetted in 20 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 70% after 1 min stirring.

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: http://www.fao.org/ag/agp/agpp/pesticid/.

3.4 **Suspensibility** (MT 184, CIPAC Handbook K, p.142, 2003. Note 2)

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, 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.

5 Storage stability

5.1 **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 that 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),
- flowability (3.7).

Note 1 Methods for the identification and determination of nicosulfuron content were adopted by CIPAC in 2005 but are not yet published in a Handbook. Prior to publication of the Handbook, copies of the methods may be obtained through the CIPAC website, http://www.cipac.org/prepubme.htm or from the CIPAC Secretary, Dr László Bura (mail to bura.laszlo@ntksz.ontsz.hu).

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 at the highest application rate of use 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 171.2, 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 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.

PART TWO

EVALUATION REPORTS

NICOSULFURON

NICOSULFURON

FAO/WHO EVALUATION REPORT 709/2005

Recommendations

The Meeting recommended that the specifications for nicosulfuron TC and WG, proposed by Du Pont, should be adopted by FAO.

Appraisal

The Meeting considered data on nicosulfuron, submitted by E.I. du Pont de Nemours, in support of proposed new FAO specifications for TC and WG. The data submitted were in accordance with the requirements of the manual (FAO/WHO 2002) and supported the draft specifications.

Nicosulfuron is a herbicide, used post-emergence in forage maize to control various annual grasses and other weeds. It is under patent in Belgium, Chile, Greece, Luxembourg and Sweden until 2007, in the USA until 2006 and in Canada until 2012.

Nicosulfuron is acidic (pKa = 4.22) and its water solubility is very dependent upon pH (407, 7100 and 46000 mg/kg at 25°C at pH 5, 7 and 9 respectively). It is stable to hydrolysis at pH 7 and 9, but hydrolyses with a half-life of 15 days at pH 5. Photolysis of nicosulfuron is quite slow.

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. The process typically produces nicosulfuron having a minimum assay of 910 g/kg. Analyses of 5 batches of nicosulfuron produced in 1998 and 1999 accounted for 99.2-99.89 % of the material (nicosulfuron 91.9-93.95%, water 4.1-4.19%, total other impurities 1.79-3.60%). These data were stated to be similar, though not identical, to those submitted for registration in the USA. For reasons beyond the control of the manufacturer and FAO, it was not possible to obtain independent confirmation from the USA authorities but the manufacturer provided details of all variations between the two sets of data (Du Pont 2006). The 5-batch analysis data provided to FAO were from a later study than the corresponding data submitted to USEPA. The proposed minimum nicosulfuron content of the TC (910 g/kg) was higher than the minimum declared for registration in the USA (885 g/kg). Four additional impurities, all <1 g/kg (and hence non-relevant) and identified in the data submitted to FAO, did not appear in the data submitted to USEPA. The manufacturing specification originally submitted to FAO was replaced with one identical to that submitted to USEPA, which was only slightly different.

The Meeting agreed that none of the impurities should be designated as relevant.

The analytical method for determination of nicosulfuron relies on reversed-phase HPLC-UV and internal standardization with diphenylmethylurea. The method was adopted by CIPAC in 2005, for the analysis of TC and WG. The HPLC method provides one identity test, with IR and UV spectrophotometry for further identification.

The draft specifications for nicosulfuron TC and WG complied with the requirements of the manual (FAO/WHO 2002).

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 709/2005

Uses

Nicosulfuron is a herbicide, which affects sensitive weeds through inhibition of the enzyme acetolactate synthase (ALS). Inhibition of ALS leads to the cessation of cell division and subsequent growth processes in plants. Rapid growth inhibition is followed by plant death. It is used post-emergence in forage maize against a variety of annual grasses and weeds.

Identity of the active ingredient

ISO common name

Nicosulfuron (E-ISO, BSI, ANSI)

Synonyms

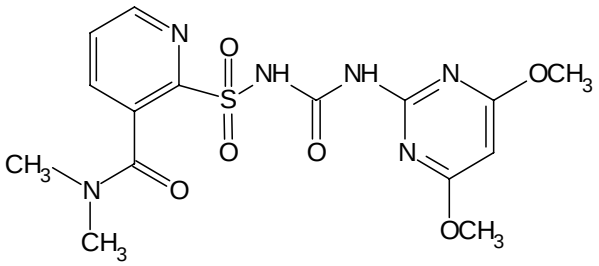
None

Chemical names

IUPAC 1-(4,6-dimethoxypyrimidin-2-yl)-3-(3-dimethylcarbamoyl-2-pyridylsulfonyl)urea

CA 2-[[[[(4,6-dimethoxyl-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]-*N*,*N*-dimethyl-3-pyridinecarboxamide

Structural formula



Empirical formula

$C_{15}H_{18}N_6O_6S$

Relative molecular mass

410.4

CAS Registry number

111991-09-4

CIPAC number

709

Identity tests

HPLC retention time; IR spectrum (page 4); UV spectrum (page 4)

Physico-chemical properties of nicosulfuron

Table 1. Physico-chemical properties of pure nicosulfuron

Parameter	Value(s) and conditions	Purity %	Method	References
Vapour pressure	1.6×10^{-14} Pa at 25ºC (extrapolated from measurements at 136.6ºC to 165.9ºC)	Not known	Knudsen gas effusion Method US EPA Pesticide Assessment Guidelines Subdivision D, Series 63-9	Knudsen 1909 USEPA 1982a AMR 1263-88
Melting point, temperature of decomposition	Melting point: 183.3 ± 0.3ºC Decomposition temperature: (colour changes) 180-190ºC	97.9	OECD 102 OPPTS 830.7200	USEPA 1996a DuPont-13183
Density	1.4222 g/cm^3 at 20ºC	97.9	OECD 109 pycnometer method OPPTS 830.7300	USEPA 1996b DuPont-13183
Solubility in water	All in buffered solutions at 25ºC* 407 mg/kg at pH 5 7.1 g/kg at pH 7 46 g/kg at pH 9	92 (mono-hydrate)	U.S. EPA Pesticide Assessment Guidelines Subdivision D, Series 63-8	USEPA 1982b V9360.D
	All in buffered solutions at 28ºC** 370 mg/l at pH 5 (4.6) 390 mg/l at pH 5 (5.1-5.6) 9.0 g/l at pH 7 (6.3) 15.0 g/l at pH 7 (6.6) 18.0 g/l at pH 9 (7.2) >250 g/l at pH 9 (9)	97.3 (mono-hydrate)	U.S. EPA Pesticide Assessment Guidelines Subdivision D, Series 63-8	AMR-1333-88
Octanol/water partition coefficient (at 25ºC)	log P K_{OW} = -0.36 at pH 5 (5.3) log P K_{OW} = -1.7 at pH 7 (7.0) log P K_{OW} = -2.2 at pH 9 (8.7)	99***	U.S. EPA Pesticide Assessment Guidelines Subdivision D, Series 63-11, shake flask method	USEPA 1982c AMR-827-87
Hydrolysis characteristics (at 25ºC, 30 d test, see also Figure 1)	Half-life = 15 days at pH 5 Stable at pH 7 Stable at pH 9	95/97 ****	U.S. EPA Pesticide Assessment Guidelines Subdivision N, Series 161-1	USEPA 1996c AMR 1104-88
Photolysis characteristics (at 25ºC, 30 d test, simulated sunlight)	Half-life = 14-19 days at pH 5 (dark control approx. 18 days) Half-life = 190-250 days at pH 7 (dark control stable) Half-life = 180-200 days at pH 9 (dark control stable)	99/98.8 *****	U.S. EPA Pesticide Assessment Guidelines Subdivision N, Series 161-2	USEPA 1996d AMR 1173-88

* Test compound was the monohydrate but results are expressed as nicosulfuron. Densities of pH 7 and 9 buffer solutions of test compound were 1.11 and 1.05 g/ml, respectively. Density of pH 5 solution not measured.

** Test compound was the monohydrate but results are expressed as nicosulfuron. Initial pH value of buffer shown, with final measured pH value in parentheses.

*** Radiopurity, pyrimidine label.

**** Radiopurity, 95% pyridine label, 97% pyrimidine label.

***** Radiopurity, 99% pyridine label, 98.8% pyrimidine label.

Table 1. Physico-chemical properties of pure nicosulfuron

Parameter	Value(s) and conditions	Purity %	Method	References
Dissociation characteristics	pKa = 4.22 at 25ºC	97.9	OECD 112, spectrophotometric method, OPPTS 830.7370	USEPA, 1996e. DuPont-13182

Figure 1. Hydrolysis of nicosulfuron at pH 5 (McFetridge, 1988)

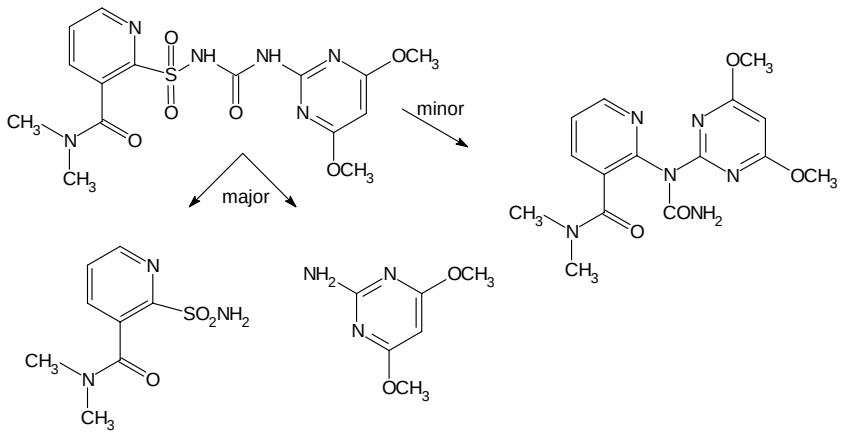


Table 2 Chemical composition and properties of technical nicosulfuron (TC)

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 99.21-99.88% and no unknowns were reported
Declared minimum nicosulfuron content	910 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 temperature of the TC	183.3°C, decomposition occurs during melting

Hazard summary

Nicosulfuron has not been evaluated by the FAO, JMPR or WHO/IPCS. A mini-dossier was submitted to Greece in 2004 and is currently under review. Nicosulfuron was submitted to the USEPA in 1990 and is currently registered in the USA.

The WHO classification of nicosulfuron is U: unlikely to cause acute hazard in normal use (WHO 2002).

Nicosulfuron does not meet the criteria established in the UN Recommendations on the Transport of Dangerous Goods (published by the United Nations Committee of Experts on the Transport of Dangerous Goods) and therefore, is not considered as dangerous or hazardous for transportation purposes.

Formulations

The main formulation type is WG, which registered and sold in several countries, worldwide. Nicosulfuron is not co-formulated with other active ingredients.

Methods of analysis and testing

Nicosulfuron is determined in the TC or WG by reversed-phase HPLC-UV, using a C-8 column and a mobile phase of water/acetonitrile, adjusted to pH 2.5 with phosphoric acid. Samples are prepared for analysis by dissolution in acetonitrile, with the addition of diphenylmethylurea as an internal standard. Nicosulfuron and the internal standard are detected at 245 nm. The method was adopted by CIPAC in 2005, following validation for analysis of the TC and both paste-extruded and dry flowable WG formulations.

Nicosulfuron may be identified by its retention volume in the HPLC method and by its UV and IR[1] spectra.

Physical properties

The physical properties, the methods for testing them and the limits proposed for the WG formulation, comply with the requirements of the manual (FAO/WHO 2002). The data in Table 7 were presented in support of the proposed specification.

Table 1. Physical testing of nicosulfuron 75 % WG prepared in April 2002 (DuPont-11469)

Test	Method	Result	
Appearance	-	Colour: light beige Odour: very slight acrid odour.	
pH of 1% aq. dispersion	CIPAC MT 75	4.5	
Bulk density (tap density)	CIPAC MT 169	0.62 g/ml	
Wettability	CIPAC 53.3.1	1 second	
Flowability	CIPAC MT 172	Product flowed spontaneously	
Storage stability at 54°C, 14 days	CIPAC MT 46.3	Ambient	After 54ºC storage, 14 d
Assay	-	75.1% ai	75.3% ai
pH	CIPAC MT 75	4.5	4.6
Wet sieve.	CIPAC MT 182	0%	0%
Suspensibility. Note 1.	CIPAC MT 168	83.4%	84.2%
Dispersibility	CIPAC MT 174	98.4%	97.6%
Persistent foam	CIPAC MT 47.2	39 ml at 1 minute	35 ml at 1 minute
Attrition resistance	CIPAC MT 178	99.3%	99.3%
Dust	CIPAC MT 171	5.7 mg (0.019%)	7.1 mg (0.02%)
Dry sieve	CIPAC MT 170	retain >90% on ~500 µm and <10% on 1410 µm	retain >90% on ~500 µm and <10% on 1410 µm

Note 1. Suspensibility: by analytical determination.

[1] A typical potassium disc should contain 0.15-0.35% by weight of nicosulfuron from the sample and the IR spectrum should not differ significantly from that of reference nicosulfuron prepared in the same way.

Containers and packaging

No special requirements for containers and packaging have been identified.

Expression of the active ingredient

The active ingredient is expressed as nicosulfuron, in g/kg.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Note: Du Pont provided written confirmation that the toxicological and ecotoxicological data included in the following summary were derived from nicosulfuron having impurity profiles similar to those referred to in Table 2, above.

Table A. Toxicology profile of nicosulfuron technical material, based on acute toxicity, irritation and sensitization

Species	Test	Duration and conditions or guideline adopted	Purity %	Result	Reference
Rat (m,f)	Acute oral	14 d, USEPA Subdivision F, 81-1 (USEPA, 1982d)	90.6	LD_{50} >5000 mg/kg bw	HLR 737-88 RV1; HLR 737-88 RV1 AD1
Rabbit, New Zealand white (m,f)	Acute dermal	14 d, USEPA Subdivision F, 81-2 (USEPA, 1982e)	90.6	LD_{50} >2000 mg/kg bw	HLR 582-87 RV1; HLR 582-87 RV1 AD1
Rat, Crl:CD BR (m,f)	Acute inhalation	4 h, ,USEPA Subdivision F, 81-3 (USEPA, 1982f)	90.6	LC_{50} >5.9 mg/l	HLR 81-88 AD1; HLR 81-88 SU1
Rabbit, New Zealand white (m)	Acute skin irritation	72 h, USEPA Subdivision F, 81-5 (USEPA, 1982g).	90.6	Non-irritant	HLR 647-87; HLR 647-87 AD1
Rabbit, New Zealand white (m)	Acute eye irritation	24 h, EEC Method B5, USEPA Subdivision F, 81-4 (USEPA, 1982h)	90.4	Non-irritant	HLR 146-87 RV1 AD1; HLR 146-87 RV1 AD2
Guinea pig, Duncan Hartley albino (m,f)	Acute skin sensitization	48 h; Buehler Method (Buehler, 1965), US EPA Subdivision F, 81-6 (USEPA, 1982i)	90.4	Not a sensitizer	HLR 429-87 RV1; HLR 429-87 RV1 AD1

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

Species	Test	Duration and conditions or guideline adopted	Purity %	Result	Reference
Rat, Cr1:CD BR (m,f)	Oral and reproductive toxicity (one generation)[1]	90 d, USEPA Subdivision F, 83-5	90.6	NOEL = 20,000 ppm (1495 and 1830 mg/kg bw/d, m & f, respectively)	HLR 15-88; HLR 15-88 AD1
Mouse, Cr1:CD-1 (ICR)BR (m,f)	Oral	90 d, USEPA Subdivision F, 82-1	90.6	NOEL = 300 ppm (43.9 and 62.3 mg/kg bw/d, m&f, respectively) [2]	HLR 16-88; HLR 16-88 AD1
Dog, beagle (m,f)	Oral	90 d, USEPA Subdivision F, 83-1	90.6	NOEL = 20,000 ppm (710 and 689 mg/kg bw/d, m&f, respectively)	HLR 332-88; HLR 332-88 AD1
Rat, Cr1:CD BR (m,f)	Oral	24 months, USEPA Subdivision F, 83-5	90.6	NOEL = 20,000 ppm (786 and 1098 mg/kg bw/d m&f, respectively)	HLR 637-89; HLR 637-89 SU AP1
Mouse, Crl/CD-1 (1CR) BR, (m,f)	Oral oncogenicity	18 months, USEPA Subdivision F, 83-2	90.6	NOEL = 7500 ppm (993 and 1312 mg/kg bw/d, m&f, respectively) [2]	HLR 645-89; HLR 645-89 SU1
Dog, beagle (m,f)	Oral feeding	1 year, USEPA Subdivision F, 83-1	90.6	NOAEL(m) = 5,000 ppm (147 mg/kg bw/d; NOAEL(f) = 20,000 ppm (587 mg/kg bw/d)	HLR 390-89
Rat, Crl:CD BR (m,f)	Reproductive toxicity (2 generations)	USEPA Subdivision F, 83-4	90.6	NOEL (parental and offspring) = 5,000 ppm (289 and 370 mg/kg bw/d m&f, respectively)	HLR 429-89
Rat, Crl:CD BR (f)	Teratogenicity study	16 d, U.S. EPA FIFRA Guideline, Subdivision F, 83-3	90.6	Non teratogenic (NOAEL) at up to 5581 mg/kg bw/day [3]	HLR 611-88; HLR 611-88 AD1

[1] The minimum requirements of USEPA guidelines were met but the study also included a 45-day clinical pathology examination and a satellite group of 10 rats/sex/dose as a one-generation reproductive range-finding study. Following the 90-day feeding phase, these animals were mated and allowed to deliver offspring, which were observed through weaning.

[2] Mean daily intake values are based on diets prepared using a purity value of 94.5%. Subsequent purity analysis by the project sponsor found the purity to be 90.6%.

[3] Mean daily intake values were recalculated based on diets prepared using the new purity value of 90.6 %

Table C. Mutagenicity profile of nicosulfuron technical material based on *in vitro* and *in vivo* tests

Species	Test	Conditions	Purity %	Result	Reference
Salmonella typhimurium	Mutagenicity	U.S. EPA Pesticide Assessment Guidelines, Subdivision F, 84-2	90.6	Negative [1]	HLR 734-88; HLR 734-88 AD1
Chinese Hamster ovary cells	CHO/HRPT gene mutation	U.S. EPA Pesticide Assessment Guidelines, Subdivision F, 84-2	90.6	Negative with and without activation	HLR 429-88; HLR 429-88 AD1
Rat hepatocytes	*In vitro* Unscheduled DNA synthesis (UDS)	U.S. EPA Pesticide Assessment Guidelines, Subdivision F, 84-2	90.6	UDS not observed	HLR 302-88; HLR 302-88 AD1
Human lymphocytes	*In vitro* gene mammalian cytogenetics	U.S. EPA Pesticide Assessment Guidelines, Subdivision F, 84-2	90.6	Negative with and without activation	HLR 470-88; HLR 470-88 AD1

[1] Subsequent reanalysis by the project sponsor found the test substance purity to be 90.6 %, not the original 94-97% as originally reported. Test results were not recalculated but this has no effect on the reported results as these were based on nominal concentration, not corrected for sample purity.

Table D. Ecotoxicology profile of nicosulfuron technical material

Species	Test	Duration and conditions	Purity %	Result	Reference
Lepomis macrochirus (bluegill sunfish)	Acute	96 h, static, U.S. EPA Pesticide Assessment Guidelines, Subdivision E, 72-1	90.6	LC_{50} >1000 mg/l *	HLR 185-88; HLR 185-88 AD1
Oncorhynchus mykiss (rainbow trout)	Acute	96 h, static, U.S. EPA Pesticide Assessment Guidelines, Subdivision E, 72-1	90.6	LC_{50} >1000 mg/l	HLR 726-8; HLR 726-87 AD1
Daphnia magna (water flea)	Acute toxicity	48 h, static, U.S. EPA Pesticide Assessment Guidelines, Subdivision E, 72-2	90.6	EC_{50} >1000 mg/l	HLR 121-88; HLR 121-88 AD1
Daphnia magna (water flea)	Chronic toxicity	21 d, static renewal, OECD Guideline 202, U.S. EPA Pesticide Assessment Guidelines, Subdivision E, 72-4	95.2	NOEC = 43 mg/l MATC = 61 mg/l LOEC = 86 mg/l EC_{50} >710 mg/l	HL-1997-01004
Lemna gibba	Growth and reproduction	14 d, FIFRA, Subdivision J, 122-2 & 123-2	92.9	Frond density: EC_{50} = 6.7 µg/l NOEC = 2.5 µg/l (Williams Test) Mean growth rate: EC_{50} = 9.0 µg/l NOEC = 2.5 µg/l (Williams Test) Biomass: EC_{50} = 7.3 µg/l NOEC = 5.0 µg/l (Kruskal-Wallis Test)	Williams 1971; Williams 1972; Sokal & Rohif 1981; AMR 2178-91
Selenastrum capricornutum (green alga)	Growth and reproduction	120 h, FIFRA, Subdivision J, 122-2 Draft Guidelines for Nontarget Plant Testing for Registration of Pesticides in Canada, Tier I	91.4	NOEC = 30 µg/l	AMR 2321-92
Eisenia foetida andrei earthworm	Acute toxicity	14 d, OECD Guideline 207	90.6	LC_{50} >1000 ppm	HUK 269/32
Apis mellifera (honey bee)	Acute oral and contact toxicity	48 h, FIFRA Subdivision L, Series 141-1, hazard evaluation: non-target insects	92.9 (oral) 97.4 (contact)	LC_{50} oral >1000 ppm (oral) LC_{50} contact >20 µg/bee	HLO 468-91 (Oral) ABM 87-3 (Contact)

* Subsequent reanalysis by the project sponsor found the test substance purity to be 90.6 %, not the original 94-97% as originally reported. Test results were not recalculated but this has no effect on the reported results as these were based on nominal concentration, not corrected for sample purity.

Table D. Ecotoxicology profile of nicosulfuron technical material

Species	Test	Duration and conditions	Purity %	Result	Reference
Colinus virginianus bobwhite quail	Acute oral toxicity	14 days Nicosulfuron technical (90.6 % purity) Pesticide Assessment Guidelines, FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms, 71-1		LD_{50} = >2250 mg/kg NOEC = 2250 mg/kg	HLO 730-8; HLO 730-87 AD1
Colinus virginianus bobwhite quail	Dietary toxicity	5 d, Pesticide Assessment Guidelines, FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms, 71-2	Not known	LC_{50} > 5620 ppm NOEC = 1780 ppm	HLO 729-87; HLO 729-87 AD1
Anas platyrhynchos Mallard duck	Dietary toxicity	5d, Pesticide Assessment Guidelines, FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms, 71-2	90.6	LC_{50} > 5620 ppm NOEC = 5620 ppm	HLO 728-87; HLO 728-87 AD1

ANNEX 2. REFERENCES

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HLR 15-88 & HLR 15-88 AD1	1989. Subchronic oral toxicity: 90-day study with IN V9360-7 feeding study and one-generation reproduction study in rats (Addendum 1).
HLR 16-88 & HLR 16-88 AD1	1989. Subchronic oral toxcity: 90-day study with IN V9360-7 feeding study in mice (Addendum 1).
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