

**FAO SPECIFICATIONS AND EVALUATIONS
FOR PLANT PROTECTION PRODUCTS**

METSULFURON METHYL

2-[3-(4-methoxy-6-methyl-[1,3,5]-triazin-2-yl-
ureidosulfonyl]benzoic acid, methyl ester

2001



TABLE OF CONTENTS
METSULFURON METHYL

	Page
DISCLAIMER	2
INTRODUCTION	3
PART ONE	
SPECIFICATION METSULFURON METHYL	
METSULFURON METHYL INFORMATION	5
METSULFURON METHYL TECHNICAL MATERIAL	6
METSULFURON METHYL WATER DISPERSIBLE GRANULES	7
METSULFURON METHYL WETTABLE POWDERS	10
PART TWO	
2001 EVALUATION REPORT METSULFURON METHYL	13

Disclaimer¹

FAO specifications are developed with the basic objective of ensuring that pesticides complying with them are satisfactory for the purpose for which they are intended so that they may serve as an international point of reference. The specifications do not constitute an endorsement or warranty of the use of a particular pesticide for a particular purpose. Neither do they constitute a warranty that pesticides complying with these specifications are suitable for the control of any given pest, or for use in a particular area. Owing to the complexity of the problems involved, the suitability of pesticides for a particular application must be decided at the national or provincial level.

Furthermore, the preparation and use of pesticides complying with these specifications are not exempted from any safety regulation or other legal or administrative provision applicable thereto. FAO shall not be liable for any injury, loss, damage or prejudice of any kind that may be suffered as a result of the preparation, transportation, sale or use of pesticides complying with these specifications. Additionally, FAO wishes to alert users of specifications to the fact that improper field mixing and/or application of pesticides can result in either a lowering or complete loss of efficacy. This holds true even where the pesticide complies with the specification. Accordingly, FAO can accept no responsibility for the consequences of improper field mixing and/or application.

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INTRODUCTION

FAO establishes and publishes specifications* for technical material and related formulations of plant protection products 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 Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent.”

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 Panel of Experts. 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 methods of synthesis. FAO has the possibility to extend the scope of the specifications to similar products, but only when the Panel of Experts 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/WAICENT/FAOINFO/AGRICULT/AGP/AGPP/Pesticid/>) or as hardcopy from the Plant Protection Information Officer.

PART ONE
SPECIFICATIONS

METSULFURON METHYL

METSULFURON METHYL INFORMATION	5
METSULFURON METHYL TECHNICAL MATERIAL	6
METSULFURON METHYL WATER DISPERSIBLE GRANULES7	
METSULFURON METHYL WETTABLE POWDERS	10

FAO SPECIFICATIONS AND EVALUATIONS FOR
PLANT PROTECTION PRODUCTS

METSULFURON METHYL

INFORMATION

ISO common name

Metsulfuron methyl (approved)

Synonyms

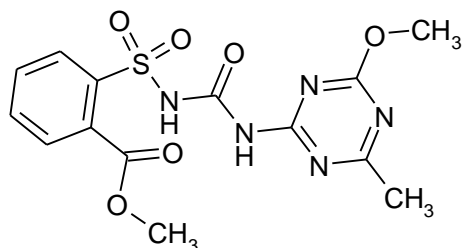
none

Chemical names

IUPAC 2-[3-(4-methoxy-6-methyl-[1,3,5]-triazin-2-yl)-ureidosulfonyl]benzoic acid, methyl ester

CA [Methyl 2-[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]=
carbonyl]amino]sulfonyl]benzoate

Structural formula



Molecular formula

C₁₄H₁₅N₅O₆S

Relative molecular mass

381.4

CAS Registry number

74223-64-6

CIPAC number

441

METSULFURON METHYL TECHNICAL MATERIAL

FAO Specification 441/TC (2001)

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 ([441/2001](#)). It should be applicable to relevant products of this manufacturer 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 ([441/2001](#)) as PART TWO forms an integral part of this publication.

1 Description

The material shall consist of metsulfuron methyl together with related manufacturing impurities and shall be an off-white to beige, homogenous, crystalline solid, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 Identity tests (CIPAC H 441/TC/M p205)

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 Metsulfuron methyl content (MT 441.3, CIPAC H, p 205)

The metsulfuron methyl content shall be declared (not less than 960 g/kg) and, when determined, the mean measured content shall not be lower than the declared minimum content.

METSULFURON METHYL WATER DISPERSIBLE GRANULES

FAO Specification 441/WG/ (2001)

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 (441/2001). It should be applicable to relevant products of this manufacturer 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 (441/2001) as PART TWO forms an integral part of this publication.

1. DESCRIPTION

The material shall consist of a homogeneous mixture of technical metsulfuron methyl, complying with the requirement of FAO Specification 441/TC 2001 together with fillers 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 (441/WG/M/3, CIPAC H p205)

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 Metsulfuron methyl content(441/WG/M/3, CIPAC H p205)

The metsulfuron methyl content shall be declared and when determined, the content obtained shall not differ from that declared by more than the following amounts:

<u>Declared content</u>	<u>Permitted tolerance</u>
above 100 up to 250 g/kg	± 6% of declared content
above 250 up to 500 g/kg	± 5% of declared content
above 500 g/kg	± 25 g/kg

4. PHYSICAL PROPERTIES

4.2 Wettability (MT 53.3.1, CIPAC F, p. 165) (Note 1)

The formulation shall be completely wetted in 60 seconds without swirling.

4.3 Wet sieve test (MT 167, CIPAC F, p. 416)

Maximum: 2.0% retained on a 75 µm test sieve.

4.4 Degree of dispersion (MT 174, CIPAC F, p. 435)

Minimum: 70% after 1 min stirring.

4.5 Suspensibility (MT 168, CIPAC F, p. 417)(Notes 2 and 3)

A minimum of 75% of the metsulfuron methyl found under 2.2 shall be in suspension after 30 minutes in CIPAC Standard Water D at 30°C ± 2°C.

4.6 Persistent foam (MT 47, CIPAC F, p. 152) (Note 4)

Maximum: 25 ml after 1 minute .

4.7 Dustiness (MT 171.1, CIPAC F, p. 425) (Note 5)

Essentially non-dusty

4.8 Flowability (MT 172, CIPAC F, p. 430)(Note 6)

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

5. STORAGE STABILITY

5.1 Stability at 54°C (MT 46.3, CIPAC J, p. 129).

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 7) and the formulation shall continue to comply with the clauses for: wet sieve test (4.3), degree of dispersion (4.4), suspensibility (4.5) and dustiness (4.7).

NOTES

Note 1 The product should be tested using 0.5 g. Although this amount of test substance is well below the 5.0 gram sample size required by the MT 53.3.1, 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 2 The MT 168 test shall be conducted using 0.1 g of the formulation

Alternatively, if the buyer requires other CIPAC Standard Waters or temperatures to be used, then this shall be specified.

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 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 0.1g.

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, 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 6 The data for the test were generated following storage at $45^{\circ}\text{C} \pm 2^{\circ}\text{C}$ for six weeks. However the product has been successfully used in hot climates.

Note 7 Analysis of the formulation, before and after the storage stability test, should be carried out concurrently (i.e. after storage) to reduce analytical error.

METSULFURON METHYL WETTABLE POWDERS

FAO Specification 441/WP/2001

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 ([441/2001](#)). It should be applicable to relevant products of this manufacturer 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 ([441/2001](#)) as PART TWO forms an integral part of this publication.

1 DESCRIPTION

The material shall consist of an homogeneous mixture of technical metsulfuron methyl (complying with 441/TC 2001) together with fillers 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: (441/TC/M/F, CIPAC H, p.205)

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

2.2 Metsulfuron methyl (441/TC/M/F, CIPAC H, p.205)

The metsulfuron methyl content shall be declared in g/kg at 20°C and, when determined, the content measured shall not differ from that declared by more than the following amounts:

<u>Declared content in g/kg at 20°C</u>	<u>Permitted Tolerance</u>
above 25 up to 100	± 10% of the declared content
above 100 up to 250	± 6% of the declared content
above 250 up to 500	± 5% of the declared content
above 500	± 25% g/kg

4 PHYSICAL PROPERTIES

4.1 Wet sieve test (MT 59.3, CIPAC F, p.179)

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

4.2 Suspensibility (MT 15.1, CIPAC F, p.45) (Notes 1, 2 and 3)

A minimum of 65 % of the metsulfuron methyl content found under 2.2 shall be in suspension after 30 min in CIPAC Standard Water D at $30 \pm 2^{\circ}\text{C}$.

4.3 Persistent foam (MT 47.1, CIPAC F, p.152)

Maximum: 25 ml after 1 minute (Note 4).

4.4 Wettability (MT 53.3.1, CIPAC F, p.165)

It shall be completely wetted in 1 minute without swirling (Note 5).

5 STORAGE STABILITY

5.1 Stability at 54°C (MT 46.1.1, CIPAC F, p.149)

After storage at $54 \pm 2^{\circ}\text{C}$ 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 (4.1), suspensibility (4.2) and wettability (4.4)

Note 1 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 chemical assay. In case of dispute, chemical assay shall be the "referee method".

Note 2 The mass of sample to be used in the test should be 0.1g.

Note 3 This test will normally only be carried out after the heat stability test

Note 4 The mass of sample to be used in the test should be 0.1g.

Note 5 The product should be tested using 0.5 g. Although this amount of test substance is well below the 5.0 gram sample size required by the MT 53.3.1, 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 analysed concurrently after the test in order to reduce the analytical error.

PART TWO
EVALUATION REPORT(S)

METSULFURON METHYL

<u>2001</u>	Evaluation report based on submission of data from E. I. du Pont de Nemours and Company (TC, WG, WP)	13
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FAO SPECIFICATIONS AND EVALUATIONS FOR
PLANT PROTECTION PRODUCTS

METSULFURON METHYL

EVALUATION REPORT 441/2001

Explanation

The data for metsulfuron methyl were evaluated in support of the review of existing FAO specifications for the Technical material (TC), and Water Dispersible Granules (WG) published in 1998 (AGP:CP/349), to include specifications for Wettable Powders (WP) as reviewed by the FAO in 1999.

Metsulfuron methyl is under patent in New Zealand, Latvia, and Lithuania until 2001, 2013, and 2013, respectively.

Metsulfuron methyl has not been evaluated by the FAO/WHO JMPR and WHO/PCS. It was evaluated/reviewed by the European Commission and was adopted into Annex I, according to Directive 91/414, on July 1, 2000. Commission Directive 2000/49/EC reflecting this decision was published in the Official Journal of the European Communities on 3 August 2000 (No. L 197, pp 32-34) and entered into force on 1 July 2001. The Annex I listing lasts for 10 years and expires on 30 June 2011.

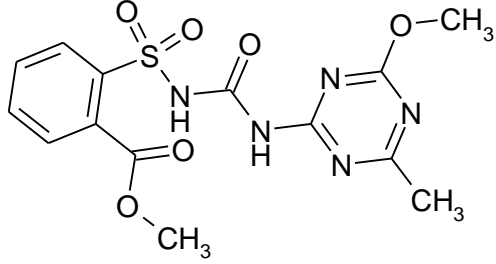
The draft specification and the supporting data were provided by E. I. du Pont de Nemours and Company in 2000. The EU review report and supporting monograph were available for the evaluation.

Uses

Metsulfuron methyl is a herbicide that inhibits the formation of acetolactate synthase (ALS inhibitor). It is used in cereals, rice, and plantation crops for the control of broadleaf weeds.

Identity

ISO common name:	Metsulfuron methyl
Chemical name(s): IUPAC	2-[3-(4-methoxy-6-methyl-[1,3,5]-triazin-2-yl-ureidosulfonyl)]benzoic acid, methyl ester
CA	Methyl 2-[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]=sulfonyl]benzoate
Synonyms	None

Structural formula	
Molecular formula	C ₁₄ H ₁₅ N ₅ O ₆ S
Relative molecular mass	381.36
CAS Registry number	74223-64-6
CIPAC number	441
Identity tests	HPLC retention time, IR

Physico-chemical properties of pure metsulfuron methyl (*Table 1*)

Parameter	Value(s) and conditions	Purity % (nominal)	Method reference (and technique if the reference gives more than one)
Vapour pressure	3.3X10 ⁻¹⁰ Pa at 25 °C (extrapolated)	99%	OECD 104, by extrapolation
Melting point, boiling point and/or temperature of decomposition	Melting point: 158-162 °C Boiling point: not applicable Decomposition temperature: decomposes upon melting	97.4%	OECD 102
Solubility in water	0.5 g/L at 25 °C at pH 5 2.8 g/L at 25 °C at pH 7 213 g/L at 25 °C at pH 9	99.4%	CIPAC MT157, Part 2, Flask Method
Octanol/water partition coefficient	log P _{OW} = 0.28 at 25 °C at pH 5 log P _{OW} = -1.74 at 25 °C at pH 7 log P _{OW} = - 2.35 at 25 °C at pH 9	97.45%	EEC A8, OECD 107, EPA OPPTS 830.7550
Hydrolysis characteristics	Half-life = 22 days at 25 °C at pH 5 Half-life = 85 days at 15 °C at pH 5 Half-life = stable for 30 days at 25 °C at pH 7 & 9 (Reference 1)	99%	EPA Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate 161-1

Photolysis characteristics	No photolysis was observed in aqueous solutions under environmental conditions (Reference 2)	99%	EPA Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate 161-2
Dissociation characteristics	pKa = 3.75	97.6 %	OECD 112, OPPTS 830.7370, spectrophotometric titration

Chemical composition and properties of metsulfuron methyl technical materials (TC and or TK) (Table 2)

Manufacturing process, maximum limits for impurities ³ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO. Mass balances were 100.3 – 100.6%.
Declared minimum a.i. content	960 g/kg
Relevant impurities ³ 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 range	158–162 °C - decomposition/gas evolution then occurs

Toxicological summaries

Notes.

(i) The proposer confirmed that the toxicological and ecotoxicological data included in the summary below were derived from metsulfuron methyl 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.

The EU review of metsulfuron methyl established the following toxicological reference doses:

ADI	0 – 0.22 mg/kg bw/day
AOEL systemic	0.7 mg/kg bw/day
AOEL dermal	20 mg/kg bw/day

Table 3. Toxicology profile of metsulfuron methyl technical material, based on acute toxicity, irritation and sensitisation.

Species	Test	Duration and conditions or guideline adopted	Result
Male and Female Rat CrI:CD®	oral	US EPA proposed guidelines for Pesticide regulation 40 CFR 163.8101 metsulfuron methyl technical (92.9% a.i.)	LD ₅₀ = >5000 mg/kg bw No deaths or clinical signs were observed.
Male and Female mouse (Crj:CD-1)	Oral	OECD Test Guideline 401 (1987) metsulfuron methyl technical (94.8% a.i.)	LD ₅₀ = >5000 mg/kg bw No deaths or clinical signs were observed.
Male and Female Rabbit (New Zealand White rabbits)	Dermal adsorption	US EPA Proposed Guidelines for Pesticide Registration 40 CFR 163.81-2 metsulfuron methyl technical (92.9% a.i.)	LD ₅₀ = >2000 mg/kg bw No deaths or clinical signs were observed.
Male and Female Rat CrI:CD®	inhalation	Haskell modified EPA guideline (24, 48, and 72 hours) metsulfuron methyl technical (95.8% a.i.)	LD ₅₀ = >5.0 mg/L No deaths occurred during the study.
Male and Female Rabbit (New Zealand White rabbits)	skin irritation	EPA Proposed Guidelines for Pesticide Registration 40 CFR 163.81-2 U.S. EPA metsulfuron methyl technical (92.9% a.i.)	Non-irritant (according to EEC Directive 93/21.)
Female Rabbit (New Zealand White rabbits)	eye irritation	Nov. 1983. "Primary Eye Irritation Study." <u>Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Humans and Domestic Animals (revised) 81-4.</u> U.S. EPA. metsulfuron methyl technical (95.8% a.i.)	Ocular non-irritant (EEC guidance [Directive 93/21])
Male and Female Guinea Pig (Duncan-Hartley albino)	skin sensitisation	U.S. EPA Pesticide Assessment Guidelines, Subdivision F, 81-6. metsulfuron methyl technical (95.8% a.i.)	No delayed hypersensitivity or allergic reactions

Table 4. Toxicology profile of the technical material based on repeated administration (subacute to chronic)

Species	Test	Duration and conditions or guideline adopted	Result [(isomer/form)]
Male and Female Rat	Subchronic 90-day feeding study	Meets requirements of US EPA FIFRA, 82-1 and EEC Directive 87/302/EEC Part B. metsulfuron methyl technical (97% a.i.)	NOEL & NOAEL = 1000 ppm (68 mg/kg bw/d for males, 84 mg/kg bw/d for females)
Male and Female Beagle dog	Subchronic 90-day feeding study	Meets requirements of US EPA, FIFRA 82-1 and ECC Directive 87/302/EEC Part B. metsulfuron methyl technical (92.9% a.i.)	NOEL = 5000 ppm (134 mg/kg/day for males and 129 mg/kg/day for females). Subchronic NOAEL > 5000 ppm (highest dose tested)
Male and Female Rat (CrI:COBS® CD® (SD)BR rats)	Chronic toxicity and potential oncogenicity	24 months metsulfuron methyl technical (93 and 95.8% a.i.)	metsulfuron methyl was not oncogenic in male or female rats. NOEL and NOAEL for chronic toxicity was 500 ppm (22.76 mg/kg/day for male and 29.97 mg/kg/day for female rats)
Male and Female Beagle dog	Chronic toxicity	52 weeks metsulfuron methyl technical (93-95.8% a.i.)	Chronic NOEL 500 ppm in males (13.28 mg/kg/day) based on decreased food consumption and 5000 ppm for females (137 mg/kg/day), the highest dose tested. The NOAEL for male and female dogs was > 5000 ppm (127 and 137 mg/kg/day, respectively) (highest dose tested)
Male and Female Rat	Effect of metsulfuron methyl on reproductive and lactation of male and female rats over two generations.	2 generation metsulfuron methyl technical (96% a.i.)	NOEL and NOAEL 500 ppm (34 and 35 mg/kg/body weight for F ₀ and F _{1B} males and females respectively; and 39 and 43 mg/kg body weight for F ₀ and F _{1B} males and females respectively, based on decreased body weights in both parental male and female rats.
Female rat (CrI:COBS® C D®(SD)BR	teratogenicity and developmental toxicity in rat	EPA Pesticide Programs Proposed Guidelines for Registering Pesticides	Maternal NOAEL was 40 mg/kg/day and developmental NOAEL was 1000 mg/kg/day or

Species	Test	Duration and conditions or guideline adopted	Result [(isomer/form)]
rats)		in the U.S.; Hazard Evaluation: Humans and Domestic Animals, Federal Register Section Series 163.3, Subpart F. metsulfuron methyl technical (92.9% a.i.)	higher. (highest dose tested)

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

Species	Test	Conditions	Result [(isomer/form)]
<i>Salmonella typhimurium</i>	<i>In vitro</i> Mutagenicity Ames Assay	Activated and non-activated rat liver (S9) metabolic systems metsulfuron methyl technical (100% a.i.)	Non-mutagenic in <i>Salmonella typhimurium</i> HLR
CHO cells	Mutagenicity CHO/HGPRT Assay	Study conducted prior to OECD guideline No. 476 and US EPA Guideline 40 CFR 798.5300, but study meets current guidelines with the exception that CO cells were used rather than LY5178Y mouse lymphoma metsulfuron methyl technical (92.9% a.i.)	metsulfuron methyl was not mutagenic in the CHO/HGPRT Assay for Gene Mutation when tested at the approximate limit of solubility, 2670 mg/L in culture medium.
Chinese hamster ovary (CHO) Cells	<i>In vitro</i> Cytogenetics Assay	The study was conducted prior to OECD guidelines. metsulfuron methyl technical (92.9% a.i.)	metsulfuron methyl induced chromosome aberrations in CHO cells exposed <i>in vitro</i> at concentrations > 1000mg/L. (highest dose tested)
Rat Primary Hepatocytes	<i>In vitro</i> Unscheduled DNA Synthesis (UDS)	Study is scientifically valid; however there is no data requirement for the <i>in vitro</i> assessment of UDS. metsulfuron methyl technical (92.9% a.i.)	metsulfuron methyl did not induce unscheduled DNA synthesis in rat hepatocytes under the conditions of the study at concentrations of 381 mg/L or less. (highest dose tested)
Mouse (bone marrow cells)	<i>In vivo</i> Micronucleus Assay	Complied with OECD No. 474. metsulfuron methyl	metsulfuron methyl did not induce micronuclei in mouse bone marrow

Species	Test	Conditions	Result [(isomer/form)]
		technical (92.9% a.i.)	polychromatic erythrocytes when administered orally at 5000 mg/kg of body weight
Rat (bone marrow cells)	<i>In vivo</i> Cytogenetic Assay	Study conducted prior to OECD guidelines but meets the principles of current guidelines. metsulfuron methyl technical (92.9% a.i.)	metsulfuron methyl did not induce chromosome aberrations in rat bone marrow when administered by oral intubation at dose rates up to 5000 mg/kg body weight.

Table 6. Ecotoxicology profile of the technical material

Species	Test	Duration and conditions	Result [(isomer/form)]
<i>Daphnia magna</i> (water flea)	Acute toxicity	OECD Guideline for testing of chemicals 202, U.S. EPA Pesticide Assessment Guidelines Subdivision E, 72-2. metsulfuron methyl 20% WG (21.0% a.i.)	48hr EC ₅₀ > 200mg a.i./L
<i>Lepomis macrochirus</i> (bluegill)	Acute toxicity	OECD Guideline for testing of chemicals 203 metsulfuron methyl technical, (93.74% a.i.)	96 hr. LC ₅₀ > 119 mg No mortality concentration 119mg/L
<i>Oncorhynchus mykiss</i> (rainbow trout)	Acute toxicity	OECD Guideline for testing of chemicals 203 metsulfuron methyl technical (93.74% a.i.)	96 hr. LC ₅₀ > 113 mg No mortality concentration 113mg/L
<i>Salmo gairdneri</i> (rainbow trout)	Flow though 21 day toxicity test	OECD Guideline for testing of chemicals 204 metsulfuron methyl technical (98.8% a.i.)	21 day EC ₅₀ & LC ₅₀ , > 150mg/L NOEC 68mg/L
[insert species, e.g. <i>Salenastrum</i> (green alga)	Effect on growth and cell count	[EU Commission Directive 92/69/EEC, Method C3 metsulfuron methyl technical (97.21% a.i.)	Healthy Cell Count EC ₅₀ 165 µg/L NOEC 50 µg/L Area Under the Growth Curve EC ₅₀ 157 µg/L NOEC 50 µg/L Growth Rate EC ₅₀ 875 µg/L NOEC 50 µg/L
<i>Eisenia foetida</i> (Earthworm)	Acute toxicity	OECD 207 metsulfuron methyl technical (100% a.i.)	14 day LC ₅₀ > 1000mg/kg
<i>Apis mellifera</i> (honey bee)	Acute oral, and contact toxicity	EPPO Guideline No. 170(1992) metsulfuron methyl technical (97.4% a.i.)	Acute oral LD ₅₀ >44.3 µg a.i./bee Acute contact LD ₅₀ >50 µg a.i./bee
<i>Colinus virginianus</i> (Bobwhite quail chicks)	Short term toxicity	Pesticide Assessment Guidelines, FIFRA, EPA-540-9-82-024 metsulfuron methyl technical (98% a.i.)	LC ₅₀ > 5620 ppm NOEL 3160 ppm
<i>Anas platyrhynchos</i>	Short term toxicity	Pesticide Assessment Guidelines, FIFRA,	LC ₅₀ > 5620 ppm

(Mallard ducklings)		EPA-540-9-82-024 metsulfuron methyl technical (98% a.i.)	NOEL 562 ppm
<i>Chrysoperla carnea</i> (Green lacewing)	Effects on beneficial arthropods	Bigler, 1988 & ESCORT, 1994 metsulfuron methyl 20% WG (19.9% a.i.)	Classified as 'harmless' Class 1 of the IOBC Categorisation (Hassan, 1992) when tested under laboratory conditions.
<i>Aphidius rhopalosiphi</i> Parasitic wasp	Effects on beneficial arthropods	Mead-Briggs, M., 1992 metsulfuron methyl 20% WG (19.9% a.i.)	Classified as 'harmless' Class 1 of the IOBC Categorisation (Hassan, 1992) when tested under laboratory conditions.
<i>Typhlodromus pyri</i> Predatory mite	Effects on beneficial arthropods	Overmeer, 1988, Lowes & Ufer, 1995 ESCORT, 1994 metsulfuron methyl 20% WG (19.9% a.i.)	Classified as 'harmless' Class 1 of the IOBC Categorisation (Hassan, 1992) when tested under laboratory conditions.
<i>Poecilus cupreus</i> Ground beetle	Effects on beneficial arthropods	IOBC Guidelines, Heimback, 1992 ESCORT 1994 metsulfuron methyl 20% WG (19.9% a.i.)	Classified as 'harmless' Class 1 of the IOBC Categorisation (Hassan, 1992) when tested under laboratory conditions.

Hazard summary

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

Metsulfuron methyl has not been classified according to WHO/PCS hazard.

N R 50/53 ECB, very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment. Classification is driven by the algae toxicity endpoint according to Annexes I, II, III, IV to Commission Directive 93/21/EEC of 27 April 1993 adapting to technical progress for the 18th time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging, and labelling of dangerous substances.

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) is CIPAC MT 441 (Reference 3). The metsulfuron methyl is determined by reversed phase HPLC, using UV detection at 254 nm and internal standardisation with phenyl sulfone. The method(s) for determination of impurities are based on reversed phase HPLC, using UV detection at 235 nm and external standardisation.

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

Physical properties

The proposer has stated 'The physical properties, the methods for testing them and the limits proposed for the WG and WP formulations, comply with the requirements of the FAO Manual (5th edition). The wettability test (CIPAC MT 53.3.1) should be conducted using a sample of 0.5 grams. Although this amount of test substance is well below the 5.0 gram sample size required by the method, 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.'

Containers and packaging

No extraordinary container or packaging issues need to be considered special requirements.

Expression of active ingredient

The active ingredient is expressed as metsulfuron methyl, methyl 2-[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl]benzoate.

Appraisal

Metsulfuron methyl is included in Annex 1 of Council Directive 91/414, and an agreed evaluation monograph, including a review report and the conditions of Annex 1 listing, was available for consultation.

Metsulfuron methyl is a post-emergence, selective sulfonyl urea herbicide acting through foliar and root uptake. It affects sensitive plants through inhibition of the enzyme acetolactate synthase. Metsulfuron methyl provides selective control over annual weeds in small grain cereals, rice, and pasture. The application rate of the substance is low, with typical application rates between 4 and 6 g ai/ha and the maximum recommended application rate in Europe of 8 g a i/ha. The application timing depends on the geographical area and crop but typically ranges between the 2 leaf stage of the crop and emergence of the flag leaf.

Metsulfuron methyl is an off-white to beige crystalline solid with a faint odour. The water solubility is pH dependent, with the highest solubility at higher pH values (0.548 g/l at pH 5 and 213 g/l at pH 9), due to the formation of the salts. The octanol:water partition coefficient is low, indicating a low potential for bio accumulation and metsulfuron methyl exhibits low vapour pressure. The technical material is not classified for explosive, oxidising or flammable properties.

The data summary submitted by the proposer in support of the physico-chemical, toxicological and ecotoxicological properties were in accordance with those evaluated

as part of the EU review of metsulfuron methyl. The Proposer confirmed that all studies submitted for this evaluation were also submitted in support of the EU review of metsulfuron methyl. Metsulfuron methyl was found to be of low acute, sub chronic and chronic toxicity. Metsulfuron methyl is rapidly eliminated from mammalian systems, mainly as the parent compound. The active substance and metabolites do not accumulate in tissues. The compound was not teratogenic and was considered by the EU review not to be genotoxic, although one test result was questioned.

Confidential information on the method of manufacture, the technical specification and data from the analysis of production batches was presented to the meeting. The proposer stated that the confidential data presented were identical to those submitted for registration in the European Union, with France as the rapporteur. Mass balances were 100.3 – 100.6% and the minimum purity of the technical material of 960 g/kg was in accordance with that considered in the EU review. Although a number of production batches showed -purities close to that of the minimum specified, the Proposer has confirmed that the figure of 960 g/kg minimum purity is appropriate to the overall production quality. is the meeting considered this to be acceptable.

The data supporting the technical material supported the TC specification as proposed.

Specifications for the WG and WP formulations were published in 1997 and 1999 respectively. The proposer has confirmed all physical properties conform to the requirements of the Manual.

Recommendations

Subject to amendments of the specifications for the water dispersible granules and wettable powders in accordance with the 5th Edition of the Manual, the meeting recommended adoption of the specifications for the technical material, water dispersible granule and wettable powder.

References

1	EPA Guidelines: Hitch, R. K., "Hydrolysis Studies", Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate 161-1, pp 44-46; October 1982; National Technical Service Information No. PB83-153973.
2	EPA Guidelines: Hitch, R. K., "Photodegradation Studies in Water", Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate 161-2, pp 46-49; October 1982; National Technical Service Information No. PB83-153973.
3	MT441.3 CIPAC H, page 205.
4	EU Review metsulfuron methyl, Commission Directive 2000/49/EC; Official Journal of the European Communities 3 August 2000 (No. L 197, pp 32-34).