FAO SPECIFICATIONS AND EVALUATIONS

FOR PLANT PROTECTION PRODUCTS

BENSULFURON-METHYL

Methyl α-(4,6-dimethoxypyrimidin-2-ylcarbamoylsulfamoyl)-*o*-toluate

2002

FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

TABLE OF CONTENTS

BENSULFURON-METHYL

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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 the Internet under (http://www.fao.org/AG/AGP/AGPP/Pesticid/) or as hardcopy from the Plant Protection Information Officer.

PART ONE

SPECIFICATIONS FOR BENSULFURON-METHYL

BENSULFURON-METHYL INFORMATION
BENSULFURON-METHYL TECHNICAL MATERIAL
BENSULFURON-METHYL WETTABLE POWDERS
BENSULFURON-METHYL WATER DISPERSIBLE GRANULES

BENSULFURON-METHYL

INFORMATION

ISO common name

Bensulfuron-methyl

Synonyms

none

Chemical names

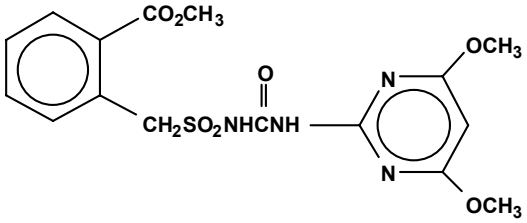
IUPAC

Methyl α-(4,6-dimethoxypyrimidin-2-ylcarbamoylsulfamoyl)-*o*-toluate

CA

Methyl 2-[[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]methyl]benzoate

Structural formula



Molecular formula

$C_{16}H_{18}N_4O_7S$

Relative molecular mass

410.4

CAS Registry number

83055-99-6

CIPAC number

502

BENSULFURON METHYL TECHNICAL MATERIAL

FAO Specification 502/TC (2002)

*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 (*502/2002*). 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 (*502/2002*) as PART TWO forms an integral part of this publication.*

1 Description

The material shall consist of bensulfuron-methyl, together with related manufacturing impurities, and shall be a white to light yellow fine crystalline solid, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (502/TC/M/ CIPAC/4181) (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 **Bensulfuron-methyl content** (502/TC/M/ CIPAC/4181) (Note 1)

The bensulfuron-methyl content shall be declared (not less than 975 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

Note 1 Method adopted by CIPAC but not yet published. Prior to publication it is available from the CIPAC secretariat on request.

FAO Specification 502/WP (2002)

*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 (*502/2002*). 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 (*502/2002*) as PART TWO forms an integral part of this publication.*

1 Description

The material shall consist of an homogenous mixture of technical bensulfuron-methyl, complying with the requirements of FAO specification 502/TC (2002), 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** (502/WP/M/, CIPAC/4258) (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 **Bensulfuron-methyl content** (502/WP/M/, CIPAC/4258) (Note 1)

The bensulfuron-methyl 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 100 up to 250 Note: the upper limit is included in this range	± 6% of the declared content

3 Physical properties

3.1 **Wet sieve test** (MT 59.3)

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

3.2 **Suspensibility** (MT 15.1, MT 177) (Note 2 and 3)

A minimum of 60% of the bensulfuron-methyl content found under 2.2 shall be in suspension after 30 min in CIPAC Standard Water D at 30 ± 2°C (Notes 4 & 5).

3.3 **Persistent foam** (MT 47.2) (Note 6)

Maximum: 60 ml after 1 minute

3.4 **Wettability** (MT 53.3.1) (Note 7)

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

4 Storage stability

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

After storage at 54 ± 2°C for 14 days, the determined average active ingredient content must not be lower than 95% relative to the determined average content found before storage (Note 8) and the formulation shall continue to comply with the clauses for:

wet sieve test (3.1);

suspensibility (3.2);

wettability (3.4).

Note 1 Method adopted by CIPAC but not yet published. Prior to publication it is available from the CIPAC secretariat on request.

Note 2 The formulation should be tested at the highest and lowest rates of use recommended by the supplier, provided this does not exceed the conditions given in methods MT 15.1 or MT 177.

Note 3 This test will normally only be carried out after the heat stability test 5.1.

Note 4 Unless another temperature is specified.

Note 5 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 6 The mass of the sample to be used in the test should be at the highest rate of use recommended by the supplier.

Note 7 The product should be tested at 0.5g. Although this amount of test substance is well below the 5.0 gram sample size required by 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 8 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.

BENSULFURON-METHYL WATER DISPERSIBLE GRANULES

FAO Specification 502/WG (2002)

*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 (*502/2002*). 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 (*502/2002*) as PART TWO forms an integral part of this publication.*

1 Description

The material shall consist of an homogenous mixture of technical bensulfuron-methyl, complying with the requirements of FAO specification 502/TC (2002), 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** (502/WG/M/ CIPAC/4181) (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 **Bensulfuron-methyl content** (502/WG/M/ CIPAC/4181) (Note 1)

The bensulfuron-methyl 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**

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

3.2 **Wet Sieve Test** (MT 167, MT 182)

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

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

Dispersibility: minimum 70% after 1 minute stirring.

3.4 **Suspensibility** (MT 168) (Notes 2 & 3)

A minimum of 60% of the bensulfuron-methyl content found under 2.2 shall be suspension after 30 minutes in CIPAC Standard Water D at 30 ± 2°C (Note 4).

3.5 **Persistent foam** (MT 47.2) (Note 5)

Maximum: 60 ml after 1 min.

3.6 **Dustiness** (MT 171) (Note 6)

Essentially non-dusty

3.7 **Flowability** (MT 172)

A minimum of 99% of the product 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)

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 (3.2);

degree of dispersion (3.3);

suspensibility (3.4);

dustiness (3.6).

Note 1 Method adopted by CIPAC but not yet published. Prior to publication it is available from the CIPAC secretariat on request.

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

Note 3 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 4 Unless another temperature is specified.

Note 5 The mass of the sample to be used in the test should be specified at the highest rate recommended by the supplier.

Note 6 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 7 Analysis of the formulation before and after storage stability test, should be carried out concurrently (i.e. after storage) to minimize the analytical error.

PART TWO

2000 EVALUATION REPORT FOR BENSULFURON-METHYL

BENSULFURON-METHYL

2002 Evaluation report based on submission of data from E.I. du Pont de Nemours and Company (TC, WP, WG)

FAO SPECIFICATIONS AND EVALUATIONS FOR
PLANT PROTECTION PRODUCTS

BENSULFURON-METHYL

EVALUATION REPORT 502/2002

Explanation

The data for bensulfuron-methyl were evaluated in support of new FAO specifications.

Bensulfuron-methyl has not been evaluated by the FAO/WHO JMPR or WHO/IPCS. Draft FAO specifications were initially presented in September 1999 and resubmission was rescheduled for September 2001. The draft specification and the supporting data were provided by E. I. du Pont de Nemours and Company in September 2001.

Bensulfuron-methyl is under patent in Greece until March 2003. A complete dossier will be submitted to the EU for evaluation in May 2004, with Italy assigned as rapporteur member state.

Uses

Bensulfuron-methyl is a selective pre-emergence and post-emergence herbicide that inhibits the formation of acetolactate synthase (ALS inhibitor). It is used in rice against many annual and perennial broadleaf weeds and sedges.

Identity

ISO common name

Bensulfuron-methyl

Chemical name(s)

IUPAC

methyl α-(4,6-dimethoxypyrimidin-2-ylcarbamoylsulfamoyl)-*o*-toluate

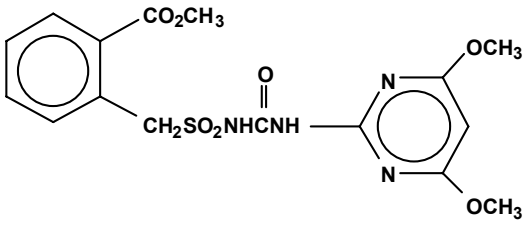
CAS

methyl 2-[[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]methyl]benzoate

Synonyms

None

Structural formula



Molecular formula

$C_{16}H_{18}N_4O_7S$

Relative molecular mass

410.4

CAS Registry number

83055-99-6

CIPAC number

502

Identity tests

HPLC retention time, IR

Table 1. Physico-chemical properties of pure bensulfuron-methyl

Parameter	Value(s) and conditions	Purity %	Method reference
Vapour pressure	2.8x 10^{-12} Pa at 25 °C (extrapolated)	99.3%	U.S. EPA Pesticide Assessment Guidelines Subdivision D, 63-9 by extrapolation; EEC method A4
Melting point, boiling point and/or temperature of decomposition	Melting point: 179.4 +/- 0.1 °C Boiling point: not applicable Decomposition temperature: 245 °C	98.3%	OECD 102 Official Journal of the European Communities, Method A.1 U.S. EPA OPPTS 830.7200
Solubility in water[b]	2.1 ppm at 25°C at pH 5 67 ppm at 25°C at pH 7 3100 ppm at 25°C at pH 9	99.5%	U.S. EPA Pesticide Assessment Guidelines Subdivision D, 63-8
Octanol/water partition coefficient	Avg K_{OW} = 160 at 25°C at pH 5 (logP 2.20) Avg K_{OW} = 6.15 at 25°C at pH 7 (logP 0.78) Avg K_{OW} = 0.102 at 25°C at pH 9 (logP –0.99)	99.5%	EEC method A8

Hydrolysis characteristics[b]	Pyrimidinyl label: Half-life = 6 days at 25°C at pH 4 Half-life = 239 days at 25°C at pH 7 Half-life = 139 days (127-151) at 25°C at pH 9 Phenyl label: Half-life = 6 days at 25°C at pH 4 Half-life = 693 days at 25°C at pH 7 Half-life = 173 days (32-313) at 25°C at pH 9	>94% and >95% for two different labels	EPA Guideline Subdivision N Chemistry: Environmental Fate 161-1 (See Reference 1) EC Directive 95/36/EC amending Council Directive 91/414/EEC SETAC, Part 1.1 OECD, Section 1, Method 111
Photolysis characteristics	Half-life = 13 days at 25°C at pH 5 (irradiated and nonirradiated solutions) Half-life = 251 and 500 days at 25°C at pH 7 (irradiated and nonirradiated solutions respectively) Half-life = 223 and 498 days at 25°C at pH 9 (irradiated and nonirradiated solutions respectively)	96.9% and 99.1% for two different labels	U.S. EPA Pesticide Assessment Guidelines Subdivision N, 161-2 (see reference 2)
Dissociation characteristics[b]	pKa = 5.2	99.0%	OECD guideline 112 12 Nohsan 8147 (Japan MAFF)

b Study results provided have not been previously reported to a regulatory agency but were considered by the WHO/PCS secretariat. The studies are scheduled to be submitted to **Italy** in May 2004.

Table 2. Chemical composition and properties of bensulfuron-methyl technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO[a]. Mass balances were 99.8 to 100.4%.
Declared minimum bensulfuron-methyl content	975 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	179 to 183 °C (decomposition starts at 245°C)

a An impurity reported to FAO (DHD34) has not been previously reported to a regulatory body. It was recently discovered as the result of improvements in chromatographic separation and product quality.

Toxicological summaries

Notes.

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

(iii) Study results provided reflect current data but additional studies are, or will soon be, in progress. The new data were not available to the JMPS but the studies are scheduled to be submitted to Italy in May 2004.

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

Species	Test	Duration and conditions or guideline adopted	Result
Male and Female Rat (Crl:CD®)	Acute oral	EEC test method B1; OECD 401 Bensulfuron-methyl technical (95.9%)	LD_{50} = > 5000 mg/kg bw
Male and Female Rabbit (New Zealand White)	Acute dermal	EEC test method B3; OECD 402 Bensulfuron-methyl technical (94%)	LD_{50} = > 2000 mg/kg bw No mortalities were observed
Male and Female Rat (Crl:CD®)	Acute inhalation	EEC test method B2; OECD 403 Bensulfuron-methyl technical (94%)	LC_{50} = >5 mg/L No mortalities were observed
Male Rabbit (New Zealand White)	Skin irritation	EEC test method B4; OECD 404 Bensulfuron-methyl technical (95.9 %)	Dermal non-irritant No clinical effects were observed
Female Rabbit (New Zealand White)	Eye irritation	EEC test method B5; OECD 405 Bensulfuron-methyl technical (95.9 %)	Ocular non-irritant
Male and Female Guinea Pig (Duncan-Hartley Albino)	Skin sensitization	EEC test method B6; OECD 406 Bensulfuron-methyl technical (96.1 %)	Non-sensitizer

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

Species	Test	Duration and conditions or guideline adopted	Result
Male and Female Rats (CD®)	Oral 90-day study	Directive 87/302/EEC part B; OECD 408 Bensulfuron-methyl technical (>95.7 %)	NOEL = 1500 ppm (or 93 and 111 mg/kg bw/day for males and females, respectively)
Male and Female Mice (CD®)	Oral 90-day study	Directive 87/302/EEC part B; OECD 408 Bensulfuron-methyl technical (>95.7 %)	NOEL = 300 ppm for males (or 39 mg/kg bw/day) and 3000 ppm for females (or 407 mg/kg bw/day)
Male and Female Beagle Dogs	Oral 90-day study	Directive 87/302/EEC part B; OECD 408 Bensulfuron-methyl technical (95.9%)	NOEL = 1000 ppm (or 32.1 and 36.3 mg/kg bw/day for males and females, respectively)
Male and Female Beagle Dogs	Oral 1-year study	Directive 87/302/EEC part B; OECD 408 Bensulfuron-methyl technical (95.9 %)	NOEL = 750 ppm (or 21.4 and 19.9 mg/kg bw/day for males and females, respectively)
Male and Female Rats	2-year chronic toxcity/oncogenicity and reproduction study	Directive 87/302/EEC part B Bensulfuron-methyl technical (95/95.9 %)	NOEL = 750 ppm for chronic toxicity and oncogenicity (or 30 and 40 mg/kg bw/day for males and females, respectively). Not oncogenic. NOEL = 7500 ppm for reproduction study (or 309 mg/kg bw/day for males and 405 mg/kg bw/day for dams and fetuses)
Male and Female Mice (Crj:CD-1)	2-year chronic toxcity and oncogenicity	Directive 87/302/EEC part B Bensulfuron-methyl technical (95.9 %)	NOEL = 2500 ppm (226 mg/kg/day for male and 227 mg/kg/day for female). Not oncogenic.
Male and Female Rats (Crl:CD®BR)	Two-generation reproductive toxicity	Directive 87/302/EEC part B Bensulfuron-methyl technical (>96%)	NOEL = 250 ppm for both parental animals and offspring (or 20 and 22 mg/kg bw/day for males and females, respectively). Not a reproductive toxin.
Female Rat (Crl:CD®(SD) BR)	Developmental toxicity	Directive 87/302/EEC part B; OECD 414 Bensulfuron-methyl technical (95%)	NOEL = 2000 mg/kg bw for the dam and for the conceptus. Non teratogenic.

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

Species	Test	Conditions	Result
Salmonella Typhimurium	*In vitro* bacterial gene mutation assay	Directive 92/69/EEC Method B14 Bensulfuron-methyl technical (95%)	Negative for mutagenic activity
Human Lymphocytes	*In vitro* cytogenics assay	Directive 92/69/EEC Method B10 Bensulfuron-methyl technical (97.3%)	Non-clastogenic with and without S9 activation
Chinese hampster ovary (CHO) cells	*In vitro* CHO/HGPRT mutation assay	Directive 87/302/EEC Part B Bensulfuron-methyl technical (95.9%)	Non-mutagenic in the presence and absence of S-9 activation system
Rat Primary Hepatocytes	*In vitro* unscheduled DNA synthesis (UDS)	Directive 87/302/EEC Part B Bensulfuron-methyl technical (95.9%)	Negative for UDS
CHO cells	*In vitro* Sister Chromatid Exchange (SCE)	Directive 87/302/EEC Part B; US EPA Pesticide Assessment Guidelines Subdivision F, 84-2 Bensulfuron-methyl technical (95.9%)	Positive results with non-activation; negative with activation
Rat (bone marrow cells) (CD®)	*In vivo micronucleus assay*	Directive 92/69/EEC Method B11 Bensulfuron-methyl technical (100 %)	Negative for induction of micronuclei at levels up to 5000 mg/kg bw

Table 6. Ecotoxicology profile of the technical material

Species	Test	Duration and conditions	Result
Daphnia magna (Water flea)	48-hour acute toxicity[b]	U.S. EPA Pesticide Assessment Guidelines Subdivision E, Section 72-2 (1982) OECD Guideline for Testing Chemicals Section 2: Effects on Biotic Systems, No. 202 (1984) EC Directive 92/69/EEC EEC Method C.2 (1992) Bensulfuron-methyl technical (98.66%)	EC_{50} = >130 ppm
Daphnia magna (Water flea)	21-day Chronic toxicity[c]	US EPA Subdivision E, 72-4, SEP EPA 540/9-846-141 Bensulfuron-methyl technical (97.3 %)	NOEL = 17 mg/L
Salmo gairdneri (Rainbow trout)	28-day bioconcentration study, flow-through	Test Guidelines not provided Bensulfuron-methyl technical (98 %)	BCF <1 during exposure phase and <2.2 during depuration in edible, non-edible or whole fish
Selenastrum capricornutum (Alga)	Growth inhibition[b]	OECD Guideline for Testing Chemicals, Section 2: Effects on Biotic Systems, No. 201 (1984) EC Directive 92/69/EEC EEC Method C3 (1992) Bensulfuron-methyl technical (98.66%)	Healthy cell count EC_{50} = 21.4 µg/l NOEC = 10 µg/l Area under the growth curve EC_{50} = 20.4 µg/l NOEC = 10 µg/l Growth rate EC_{50} = 57.4 µg/l NOEC = 40 µg/l
Anabaena flos-aquae (Alga)	Growth inhibition[b]	US EPA OPPTS 850.5400 (1996) Bensulfuron-methyl technical (98.66%)	Healthy cell count EC_{50} = 50.6 µg/l NOEC = 31.25 µg/l Area under the growth curve EC_{50} = 44.1 µg/l NOEC = 31.25 µg/l Growth rate EC_{50} = 88.5 µg/l NOEC = 125 µg/l
Eisenia Fetida (Earthworm)	14-day Acute toxicity[b]	OECD – 207, 1984 and ISO 11268, part 1, 1993 Bensulfuron-methyl technical (98.66 %)	LC_{50} and LOEC = >1000 mg/kg

Apis mellifera (Honey bee)	Acute contact toxicity[c]	EPPO guideline 170 Bensulfuron-methyl technical (95.9%)	LD_{50} of >12.5 µg/bee
Salmo gairdneri (Rainbow trout)	96-hr. Acute toxicity[b]	U.S. EPA Pesticide Assessment Guidelines Subdivision E, Section 72-1 (1982) OECD Guideline for Testing Chemicals Section 2: Effects on Biotic Systems, No. 203 (1992) EC Directive 92/69/EEC EEC Method C.1 (1992) Bensulfuron-methyl technical (98.66%)	LC_{50} of >66 mg/L
Lepomis Macrochirus (Bluegill sunfish)	96-hr. Acute toxicity[b]	U.S. EPA Pesticide Assessment Guidelines Subdivision E, Section 72-1 (1982) OECD Guideline for Testing Chemicals Section 2: Effects on Biotic Systems, No. 203 (1992) EC Directive 92/69/EEC EEC Method C.1 (1992) Bensulfuron-methyl technical (98.66%)	LC_{50} of >120 mg/L
Anas Platyrhynchos (Mallard duck chicks)	5-day Dietary study	ASTM Standard E857-81 and ESEPA FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms (see reference 4) Bensulfuron-methyl technical (95.9%)	LC_{50} of > 5620 ppm NOEL = 1000 ppm No mortalities observed
Anas Platyrhynchos (Male and female mallard ducks)	Acute oral toxicity	Pesticide Assessment guidelines, FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms (see reference 5) Bensulfuron-methyl technical (95.9 %)	LD_{50}= > 2510 mg/kg
Anas Platyrhynchos (Male and female mallard ducks)	One generation reproduction study[c]	US EPA FIFRA Subdivision E, Section 71-4 and OECD Guideline 206 Bensulfuron-methyl technical (98.66 %)	NOEC = 520 mg/kg feed (highest rate tested)

b Study results provided have not been previously reported to a regulatory agency but were considered by the WHO/PCS secretariat. The studies are scheduled to be submitted to Spain in May 2003.

Bensulfuron-methyl has not been evaluated by the WHO IPCS or by the FAO/WHO JMPR and it has not been classified according to IPCS hazard. Bensulfuron-methyl does not exceed the criteria established in the 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/hazardous for transportation purposes.

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 methods for the active ingredient (including identity tests) are 502/TC/M/, 502/WG/M/ (CIPAC/4181) and 502/WP/M/, (CIPAC/4258), (full CIPAC methods) (reference 5). The bensulfuron-methyl is determined by reversed-phase HPLC, using UV detection at 236 nm and internal standardisation. The methods 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, EPA, EEC, and CIPAC 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 WP and WG formulations, comply with the requirements of the FAO Manual (5^{th} 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 in far excess of the maximum concentration recommended for use. However, it is a sufficient quantity to enable an accurate visual determination of wettability.

Containers and packaging

There are no special container or packaging requirements.

Expression of the active ingredient

The active ingredient is expressed as bensulfuron-methyl.

Appraisal

Bensulfuron-methyl exhibits low vapour pressure, the water solubility is pH-dependent, with the highest solubility at higher pH values due to the formation of water-soluble salts (2.1 mg/l at pH 5 and 3100 mg/l at pH 9). Bensulfuron-methyl hydrolyses rapidly at pH 4 but is stable at pH 7 and 9 at 25°C. Cleavage of the sulfonylurea linkage is the primary hydrolytic degradation pathway. The photolysis characteristics are pH dependent. At pH 4, hydrolysis is so much more rapid than the slow photolysis that photolysis makes no significant

contribution to the rate of degradation under these conditions. Bensulfuron-methyl is stable to direct photolysis in sterile buffer solutions, but degrades rapidly via cleavage of the sulfonylurea linkage in natural water under sunlight. The apparent difference in hydrolysis rates observed in the "dark photolysis" and "hydrolysis" studies is not significant due to the variability in results obtained in the studies and the consequent errors in estimation of hydrolysis half-life. The octanol:water partition coefficient indicates a low potential for bio-accumulation. The technical material is not classified for explosive, oxidising or flammable properties.

Bensulfuron-methyl is a systemic sulfonylurea herbicide for the pre- and post emergence control of annual and perennial broad-leaved and sedge weeds in rice. Bensulfuron methyl is selective acting, through foliar and root uptake, by inhibiting biosynthesis of the essential amino acids valine and isoleucine. It stops cell division by inhibition of the acetolactate synthase enzyme. The application rate of the substance is low, with typical application rates of 50 to 60 g ai/ha. The application timing depends on the geographical area and is typically applied at 2- to 3-leaf stage of the rice.

The data submitted were in accordance with the requirements of the FAO Manual (5^{th} edition) and supported the draft specifications.

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 Hungarian registration of bensulfuron-methyl, except for certain study results that have not been previously reported to a regulatory agency and are considered new data (namely: solubility in water; hydrolysis characteristics; dissociation characteristics; water flea 48-hour acute toxicity; algal growth inhibition; earthworm 14-day acute toxicity; rainbow trout 96-hr. acute toxicity; bluegill sunfish 96-hr. acute toxicity; honey bee acute contact toxicity; male and female mallard ducks 1-generation reproduction study).

These studies are scheduled to be submitted to the EU in May 2004 in support of a new EU registration and were considered by the WHO/PCS secretariat for the present evaluation. The PCS secretariat 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 in in support of the proposed specifications. In the opinion of WHO/PCS, the apparent discrepancies in the hydrolysis characteristics presented in Table 1 were due to the fact that in the experiment, performed in accordance with the OECD guideline, the longest hydrolysis time studied was 30 days, and thus any half-life reported in excess of approximately 200 days is very uncertain (<10% hydrolysis) and all such half-lives in the table should be considered to be >200d.

The main formulation types available are water dispersible granules (WG) and wettable powders (WP).

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, except for the recently discovered impurity, DHD34, discovered as the result of improved chromatographic separations. Among the impurities included in the data package initially submitted to FAO in October 2001, were four

compounds identified as JF987, L8399, F6135 and KW557, which had only been included for the purpose of manufacturing quality control limits at 1 g/kg. As these non-relevant impurities always appear at levels well below the 1 g/kg limit, and are only used as process monitoring tools, the meeting diregarded them. Mass balances were 99.8 – 100.4 % and the minimum purity of the technical material of the two production plants was 990 g/kg, according to the 10-batch data.

The purity of the technical material used in the toxicological studies was 94-98.66%. The improvements in overall efficiency of manufacture has translated into a material with higher minimum purity. (96.5% to 97.5%). As the overall process has remained the same, the impurity profile on a qualitative basis also remains unchanged.

The proposer considered the technical material used in recent studies to be both historically representaive of bensulfuron-methyl synthesis processes as well as directly representative of material that is currently being distributed and sold commercially.

Bensulfuron-methyl is of low acute, subacute and chronic toxicity. It is rapidly metabolised and eliminated from mammalian systems; the primary metabolic pathway include hydroxilation and *O*-demethylation. The active substance and metabolites do not accumulate in tissues. Bensulfuron-methyl is non-irritant to eyes and not skin sensitizing. The compound is non-teratogenic and is not considered to be a mutagen.

Bensulfuron-methyl has not been evaluated by the WHO IPCS or by the FAO/WHO JMPR. The IPCS hazard classification is: “unlikely to present acute hazard in normal use". The WHO toxicity class (a.i.) is III, the EPA toxicity class (formulation) is IV. The classification following EU is Xi (R43).

Bensulfuron-methyl is very toxic to aquatic organisms (N R 50/53 ECB) and 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. Bensulfuron-methyl is moderately toxic to honey bees, but in normal use is unlikely that there will be significant risks to bees.

The HPLC method for bensulfuron-methyl TC and WG formulations CIPAC/4181, and the method for WP formulations, CIPAC/4258, have been adopted as full CIPAC methods. (CIPAC/4265/P). 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 draft specifications for the bensulfuron-methyl technical material, water dispersible granules and wettable powders should be adopted by FAO.

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	ASTM Standard E857-81, Standard Practice for Conducting Subacute Dietary Toxicity Tests with Avian Species, " American Society for Testing and Materials, 1982.
4	Anonymous, Pesticide Assessment Guidelines, FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms, subsection 71-2, Environmental Protection Agency, Office of Pesticide Programs, October 1982.
5	CIPAC meeting minutes, June 2001, www.cipac.org, under unpublished methods. CIPAC meeting minutes, June 2002, www.cipac.org, under unpublished methods
6	C. D. S. Tomlin, Ed., The pesticide manual, 11th edn, 1997, BCPC, Farnham, UK
7	Bensulfuron methyl at: http://www.rsc.org/pdf/general/12bensul.pdf
8	Summary of the decisions taken at the 45th CIPAC meeting in Bangkok, 2001,CIPAC/4265/P
9	Summary of the decisions taken at the 46th CIPAC meeting in Rome, 2002, CIPAC/4312/P
10	IPCS, the WHO recommended classification of pesticides by hazard and guidelines to classification 1998-1999. WHO/PCS/98.21/Rev. 1.