

**FAO SPECIFICATIONS AND EVALUATIONS  
FOR AGRICULTURAL PESTICIDES**

**ETHOFUMESATE**

2007

**(±)-2-ethoxy-2,3-dihydro-3,3-dimethylbenzofuran-  
5-yl methanesulfonate**



**Food and Agriculture Organization  
of the United Nations**

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## DISCLAIMER<sup>1</sup>

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

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

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

FAO disclaims any and all liability for any injury, death, loss, damage or other prejudice of any kind that may arise as a result of, or in connection with, the manufacture, sale, transportation, storage, handling, preparation and/or use of pesticides which are found, or are claimed, to have been manufactured to comply with these specifications.

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<sup>1</sup> This disclaimer applies to all specifications published by FAO.

## INTRODUCTION

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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 5<sup>th</sup> 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 5<sup>th</sup> 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/pest-and-pesticide-management/en/>

OR IN HARDCOPY FROM THE PLANT PROTECTION INFORMATION OFFICER.

## **PART ONE**

### **SPECIFICATIONS**

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## ETHOFUMESATE

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### INFORMATION

*ISO common names*

ethofumesate (E-ISO, (m) F-ISO, BSI, ANSI, WSSA)

*Synonyms*

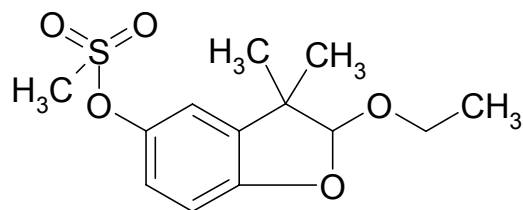
none

*Chemical names*

*IUPAC* (±)-2-ethoxy-2,3-dihydro-3,3-dimethylbenzofuran-5-yl  
methanesulfonate

*CA* 5-benzofuranol, 2-ethoxy-2,3-dihydro-3,3-dimethylmethanesulfonate

*Structural formula*



*Empirical formula*

C<sub>13</sub>H<sub>18</sub>O<sub>5</sub>S

*Relative molecular mass*

286.3

*CAS Registry number*

26225-79-6

*CIPAC number*

233

*Identity tests*

HPLC retention time, IR, NMR

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## ETHOFUMESATE TECHNICAL MATERIAL

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### FAO Specification 233/TC (January 2007\*)

*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 (233/2005). It should be applicable to relevant products of the company but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report, (233/2005) as PART TWO, forms an integral part of this publication.*

#### 1 Description

The material shall consist of ethofumesate, together with related manufacturing impurities, and shall be a buff to brown solid, free from visible extraneous matter and added modifying agents.

#### 2 Active ingredient

##### 2.1 Identity tests (233/TC/M/2, CIPAC Handbook J, p.44, 2000)

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 Ethofumesate content (233/TC/M/3, CIPAC Handbook J, p.44, 2000)

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

#### 3 Relevant impurities (Note 1)

##### 3.1 Water (MT 30.5, CIPAC Handbook J, p.120, 2000)

Maximum: 5 g/kg.

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**Note 1** There are no relevant impurities to be controlled in products of the manufacturer identified in evaluation report 233/2005. However, ethyl methane sulfonate and/or iso-butyl methane sulfonate can occur as a result of certain manufacturing processes. If these impurities could occur at  $\geq 0.1$  mg/kg (relative to ethofumesate) in the products of other manufacturers, they would be designated as relevant impurities and clauses would be required to limit their concentration.

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/pest-and-pesticide-management/en/>

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## ETHOFUMESATE EMULSIFIABLE CONCENTRATE

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### FAO Specification 233/EC (January 2007\*)

*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 (233/2005). It should be applicable to relevant products of the company but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report, (233/2005) as PART TWO, forms an integral part of this publication.*

## 1 Description

The material shall consist of technical ethofumesate, complying with the requirements of FAO specification 233/TC (January 2007), dissolved in suitable solvents, together with any other necessary formulants. It shall be in the form of a stable homogeneous brownish liquid, free from visible suspended matter and sediment, to be applied as an emulsion after dilution in water.

## 2 Active ingredient

### 2.1 Identity tests (233/EC/M/2, CIPAC Handbook J, p.49, 2000)

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 Ethofumesate content (233/EC/M/3, CIPAC Handbook J, p.49, 2000)

The ethofumesate content shall be declared (g/kg or g/l at  $20 \pm 2^\circ\text{C}$ , Note 1) and, when determined, the average content measured shall not differ from that declared by more than the following tolerances:

Declared content in g/kg or g/l at $20 \pm 2^\circ\text{C}$	Tolerance
above 100 up to 250	$\pm 6\%$ of the declared content
Note: the upper limit is included in the range	

## 3 Relevant impurities (Note 2)

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/pest-and-pesticide-management/en/>



## 4 Physical properties

### 4.1 Emulsion stability and re-emulsification (MT 36.3, CIPAC Handbook K, p.137, 2003) (Note 3)

The formulation, when diluted at  $30 \pm 2^\circ\text{C}$  (Notes 4) with CIPAC standard waters A and D, shall comply with the following:

Time after dilution	Limits of stability, MT 36.3
0 h	Initial emulsification complete
0.5 h	"Cream", maximum: 0.5 ml
2.0 h	"Cream", maximum: 1 ml "Free oil": none
24 h	Re-emulsification complete
24.5 h	"Cream", maximum: 2 ml "Free oil": none
Note: tests after 24 h are required only where results at 2 h are in doubt	

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

Maximum: 60 ml after 1 min.

## 5 Storage stability

### 5.1 Stability at $0^\circ\text{C}$ (MT 39.3, CIPAC Handbook J, p.126, 2000)

After storage at  $0 \pm 2^\circ\text{C}$  for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

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

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 5), and the formulation shall continue to comply with the clause for:

- emulsion stability and re-emulsification (4.1).

**Note 1** If the buyer requires both g/kg and g/l at  $20^\circ\text{C}$ , then in case of dispute the analytical results shall be calculated as g/kg.

**Note 2** There are no relevant impurities to be controlled in products of the manufacturer identified in evaluation report 233/2005. However, ethyl methane sulfonate and/or iso-butyl methane sulfonate can occur as a result of certain manufacturing processes. If these impurities could occur at  $\geq 0.1$  mg/kg (relative to ethofumesate) in the products of other manufacturers, they would be designated as relevant impurities and clauses would be required to limit their concentration.

**Note 3** This test will normally only be carried out after the heat stability test, 5.2.

**Note 4** The test should be carried out at the highest application concentration.

Note 5 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.

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## ETHOFUMESATE AQUEOUS SUSPENSION CONCENTRATE

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### FAO Specification 233/SC (January 2007\*)

*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 (233/2005). It should be applicable to relevant products of the company but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report, (233/2005) as PART TWO, forms an integral part of this publication.*

## 1 Description

The material shall consist of a suspension of fine particles of technical ethofumesate, complying with the requirements of FAO specification 233/TC (January 2007), in an aqueous phase together with suitable formulants. After gentle agitation the material shall be homogeneous (Note 1) and suitable for further dilution in water.

## 2 Active ingredient

### 2.1 Identity tests (233/SC/M/2, CIPAC Handbook J, p.48, 2000)

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 Ethofumesate content (233/SC/M/3, CIPAC Handbook J, p.48, 2000)

The ethofumesate content shall be declared (g/kg or g/l at  $20 \pm 2^\circ\text{C}$ , Note 2) and, when determined, the average content measured shall not differ from that declared by more than the following tolerances:

Declared content in g/kg or g/l at $20 \pm 2^\circ\text{C}$	Tolerance
above 100 up to 250	$\pm 6\%$ of the declared content
above 250 up to 500	$\pm 5\%$ of the declared content
Note: in each range the upper limit is included	

## 3 Relevant impurities (Note 3)

## 4 Physical properties

### 4.1 Pourability (MT 148, CIPAC Handbook F, p.348, 1995)

Maximum "residue": 5%.

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/pest-and-pesticide-management/en/>

**4.2 Spontaneity of dispersion** (MT 160, CIPAC Handbook F, p.391, 1995)  
(Note 4)

A minimum of 90% of the ethofumesate content found under 2.2 shall be in suspension after 5 min in CIPAC standard water D at  $30 \pm 2^\circ\text{C}$ .

**4.3 Suspensibility** (MT 184, CIPAC Handbook K, p.142, 2003) (Note 4)

A minimum of 90% of the ethofumesate content found under 2.2 shall be in suspension after 30 min in CIPAC standard water D at  $30 \pm 2^\circ\text{C}$ .

**4.4 Wet sieve test** (MT 185, CIPAC Handbook K, p.148, 2003) (Note 5)

Maximum: 2% of the formulation shall be retained on a 75  $\mu\text{m}$  test sieve.

**4.5 Persistent foam** (MT 47.2, CIPAC Handbook F, p.152, 1995) (Note 6)

Maximum: 60 ml after 1 min.

**5 Storage stability**

**5.1 Stability at  $0^\circ\text{C}$**  (MT 39.3, CIPAC Handbook J, p.126, 2000)

After storage at  $0 \pm 2^\circ\text{C}$  for 7 days, the formulation shall continue to comply with clauses for:

- suspensibility (4.3),
- wet sieve test (4.4).

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

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 7), and the formulation shall continue to comply with the clauses for:

- pourability (4.1),
- spontaneity of dispersion (4.2),
- suspensibility (4.3),
- wet sieve test (4.4)

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**Note 1** Before sampling to verify the formulation quality, inspect the commercial container carefully. On standing, suspension concentrates usually develop a concentration gradient from the top to the bottom of the container. This may even result in the appearance of a clear liquid on the top and/or of sediment on the bottom. Therefore, before sampling, homogenize the formulation according to the instructions given by the manufacturer or, in the absence of such instructions, by gentle shaking of the commercial container (for example by inverting the closed container several times). Large containers must be opened and stirred adequately. After this procedure, the container should not contain a sticky layer of non-dispersed matter at the bottom. A suitable and simple method of checking for a non-dispersed sticky layer "cake" is by probing with a glass rod or similar device adapted to the size and shape of the container. All the physical and chemical tests must be carried out on a laboratory sample taken after the recommended homogenization procedure.

**Note 2** Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the mass per millilitre and in calculation of the active ingredient content (in g/l) if methods other than MT 3.3 are used. If the buyer requires both g/kg and g/l at  $20^\circ\text{C}$ , then in case of dispute the analytical results shall be calculated as g/kg.

**Note 3** There are no relevant impurities to be controlled in products of the manufacturer identified in evaluation report 233/2005. However, ethyl methane sulfonate and/or iso-butyl methane

sulfonate can occur as a result of certain manufacturing processes. If these impurities could occur at  $\geq 0.1$  mg/kg (relative to ethofumesate) in the products of other manufacturers, they would be designated as relevant impurities and clauses would be required to limit their concentration.

Note 4 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, simpler methods such as gravimetric and solvent extraction determination may be used on a routine basis provided that these methods have been shown to give equal results to those of the chemical assay method. In case of dispute, the chemical method shall be the referee method.

Note 5 This test detects coarse particles (e.g. caused by crystal growth) or agglomerates (crust formation) or extraneous materials which could cause blockage of spray nozzles or filters in the spray tank.

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

Note 7 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.

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## ETHOFUMESATE AQUEOUS SUSPO-EMULSION

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### FAO Specification 233/SE (January 2007\*)

*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 (233/2005). It should be applicable to relevant products of the company but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation report, (233/2005) as PART TWO, forms an integral part of this publication.*

## 1 Description

The material shall consist of: **either** a suspension of fine particles of technical ethofumesate, complying with the requirements of FAO specification 233/TC (January 2007) combined with an emulsion of fine droplets of a 2<sup>nd</sup> active ingredient, in an aqueous phase together with suitable formulants; **or** an emulsion of technical ethofumesate, complying with the requirements of FAO specification 233/TC (January 2007), together with a suspension of fine particles of a 2<sup>nd</sup> active ingredient, in an aqueous phase together with suitable formulants. After gentle agitation, the material shall appear homogeneous (Note 1) and be suitable for further dilution in water.

## 2 Active ingredient

### 2.1 Identity tests (233/SE/M/2, CIPAC Handbook L, p.80, 2005)

The active ingredients shall comply with identity tests and, where an identity remains in doubt, it shall comply with at least one additional test.

### 2.2 Ethofumesate content (233/SE/M/3 CIPAC Handbook J, p.80, 2005)

The ethofumesate content shall be declared (g/kg or g/l at 20 ± 2°C, Note 2) and, when determined, the average contents measured shall not differ from those declared by more than the following tolerances:

Declared content in g/kg or g/l at 20 ± 2°C	Tolerance
above 25 up to 100	± 10% of the declared content
Note: the upper limit is included in the range	

## 3 Relevant impurities (Note 3)

## 4 Physical properties

### 4.1 Pourability (MT 148, CIPAC Handbook F, p.348, 1995)

Maximum "residue": 2%.

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\* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: <http://www.fao.org/pest-and-pesticide-management/en/>

**4.2 Dispersion stability** (MT 180, CIPAC Handbook H, p.310, 1998) (Note 4)

The formulation, when diluted at  $30 \pm 2^\circ\text{C}$  with CIPAC standard waters A and D, shall continue to comply with the following:

Time after allowing the dispersion to stand	Limits of stability
0 h	Initial dispersion complete
0.5 h	"Cream", maximum: 0.5 ml "Free oil": none Sediment, maximum: 0.1 ml
24 h	Re-dispersion complete
24.5 h	"Cream", maximum: 2 ml "Free oil": none Sediment, maximum: 0.1 ml

**4.3 Wet sieve test** (MT 185, CIPAC Handbook K, p.148, 2003) (Note 5)

Maximum: 2% of the formulation shall be retained on a 75  $\mu\text{m}$  test sieve at the dilutions specified.

**4.4 Persistent foam** (MT 47.2, CIPAC Handbook F, p.152, 1995) (Note 6)

Maximum: 60 ml after 1 min.

**5 Storage stability**

**5.1 Stability at  $0^\circ\text{C}$**  (MT 39.3, CIPAC Handbook J, p.126, 2000)

After storage at  $0 \pm 2^\circ\text{C}$  for 7 days, the formulation shall continue to comply with the clauses for:

- dispersion stability (4.2),
- wet sieve test (4.3).

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

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 7), and the formulation shall continue to comply with the clauses for:

- pourability (4.1),
- dispersion stability (4.2),
- wet sieve test (4.3).

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**Note 1** Before sampling to verify formulation quality, inspect the commercial container carefully. On standing, suspo-emulsions usually develop a concentration gradient which may result in the appearance of a clear layer at either the top or the bottom of the container. A sediment layer may also form at the bottom of the container, which can be detected by probing with a glass rod. Before sampling, homogenize the formulation according to the instructions given by the manufacturer or, in the absence of such instructions, by gentle shaking of the commercial container (for example by inverting the closed container several times).

After this procedure the container should not contain a sticky layer of non-dispersed matter at the bottom (if the suspo-emulsion has flocculated it may not be possible to re-disperse this sticky layer). All the physical and chemical tests must be carried out on a laboratory sample taken after the recommended homogenization procedure.

Note 2 Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the active ingredient content in g/l. It is preferable, therefore, to determine the content in g/kg and, if necessary, to determine the mass per millilitre, to calculate the active ingredient content in g/l.

Note 3 There are no relevant impurities to be controlled in products of the manufacturer identified in evaluation report 233/2005. However, ethyl methane sulfonate and/or iso-butyl methane sulfonate can occur as a result of certain manufacturing processes. If these impurities could occur at  $\geq 0.1$  mg/kg (relative to ethofumesate) in the products of other manufacturers, they would be designated as relevant impurities and clauses would be required to limit their concentration.

Note 4 This test will normally be carried out after the stability at elevated temperatures test (7.41.5.2). The test should be carried out at the highest and lowest recommended rates of use.

Note 5 This test detects oversize particles (e.g. caused by crystal growth) or flocs (formed between the suspension particles and the emulsion oil phase), or extraneous material, which could cause blockage of spray nozzles or filters in the spray tank. The test should be conducted at the lowest and highest rates of dilution recommended for use.

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

Note 7 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.



PART TWO

EVALUATION REPORTS

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ETHOFUMESATE

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## ETHOFUMESATE

### FAO/WHO EVALUATION REPORT 233/2005

#### Recommendations

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The Meeting recommended the following.

- (i) The new specifications for ethofumesate TC, EC, SC and SE, proposed by Bayer CropScience and as amended, should be adopted by FAO.
- (ii) The new specification for ethofumesate OD, proposed by Bayer CropScience and as amended, should be adopted by FAO subject to CIPAC adoption of the extension to the method for determination of ethofumesate content.

#### Appraisal

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Data for ethofumesate were submitted by Bayer CropScience in support of proposed new FAO specifications for TC, EC, SC, SE and OD. The data submitted were in accordance with the requirements of the manual (FAO/WHO, 2002)

Ethofumesate is not under patent.

Ethofumesate is of low volatility and has low solubility in water but is readily soluble in organic solvents. Hydrolysis is extremely slow at pH 5 and does not occur at pH 7 or 9. Photolysis is also slow. Ethofumesate has no acidic or basic characteristics.

The Meeting was provided with commercially confidential information on the manufacturing process and 5-batch analysis data on all impurities present at or above 1 g/kg. Mass balances were high: 98.9-99.5%. The data were confirmed as being similar to those submitted for registration in the UK.

The manufacturer proposed that methanesulfonic acid, ethyl ester (EMS) and methanesulfonic acid, 2-methylpropyl ester (iBMS) should be designated as relevant impurities, with a limit of <0.1 mg/kg in each case. WHO/PCS confirmed that, as potent mutagens, EMS and iBMS compounds would qualify as relevant impurities at <1 g/kg. The manufacturer confirmed that, since commencing production in 1976, the manufacturing plant had employed process steps which ensured that both impurities remained essentially undetectable by analysis, using a method with a limit of quantification of 0.1 mg/kg.

The Meeting acknowledged that the hazards associated with EMS and iBMS make them candidates for designation as relevant impurities but considered that, as they are undetectable in practice, they should be designated as non-relevant. This convention of JMPS is explained in the 2006 revision of the manual (FAO/WHO 2006). WHO/PCS welcomed the manufacturer's stringent control of EMS and iBMS but observed that the maximum limits acceptable under the GHS guidelines (GHS 2003) would be 1 g/kg. The manufacturer stated that the company had detected relatively high levels of EMS and iBMS in ethofumesate from certain other sources and the Meeting agreed that it was necessary to alert buyers and users to the possibility that they may occur at measurable levels in other products. The Meeting therefore agreed that footnotes should be appended to the specifications, drawing

attention to the possibility that measurable levels of EMS and iBMS may occur in the products of other manufacturers.

The Meeting considered the proposed specifications which, with the exception of a few issues described below, were generally in accordance with the requirements of the manual (FAO/WHO 2002).

TC. The Meeting agreed with the proposal to designate water as a relevant impurity, on the basis that the TC is used to prepare ECs (ethofumesate is not prone to hydrolysis).

SC, SE and OD. The manufacturer proposed clauses for wet sieving based on the use of a 150 µm test sieve, with limits of 0.01% retention on the sieve. The standard test sieve adopted for FAO/WHO specifications is 75 µm but the manufacturer stated that the larger mesh is more representative of typical filters and nozzles used in the application equipment. The Meeting did not accept this argument and the manufacturer indicated that 2% limits would be appropriate for tests made with the standard 75 µm test sieve.

SE. The manufacturer stated that ethofumesate may be present in suspension or emulsion form, according to the product and co-formulated active ingredient. The Meeting considered it likely that some degree of equilibration must occur between the three phases but accepted that the description clause should encompass ethofumesate SEs of both types.

Analytical methods for determination of ethofumesate in TC, EC, SC and SE are full CIPAC methods. The methods are based on HPLC with UV detection and the retention time provides the primary identification. IR and NMR spectra may also be used for identification. Extension of the methods to analysis of OD has not yet been validated through CIPAC.

Analytical methods for the determination of impurities are based on HPLC with UV detection and external standardization, GC-FID with internal standardization, or in the case of EMS and iBMS, by a peer-validated GC-MS/SIM method.

Test methods for determination of physico-chemical properties of the active ingredient were OECD, EPA or EC, whereas those for the formulations were CIPAC, as indicated in the specifications.

**SUPPORTING INFORMATION  
FOR  
EVALUATION REPORT 233/2005**

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## Uses

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Ethofumesate is a selective systemic herbicide, absorbed by the emerging shoots (grasses) or roots (broad-leaved plants), with translocation to the foliage. It is not readily absorbed by leaves after the plant has generated a mature cuticle. Ethofumesate inhibits the growth of meristems, retards cellular division, and limits formation of waxy cuticles. It is used pre- and/or post-emergence in sugar beet and other beet crops, turf, ryegrass and the other pasture grasses, at 0.3-2.0 kg a.i./ha against a wide range of grass and broad-leaved weeds, with persistence of activity in the soil. Some crops are highly tolerant towards ethofumesate, including strawberries, sunflowers, Phaseolus beans and tobacco, depending on the time of application.

## Identity

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### ISO common names

ethofumesate (E-ISO, (m) F-ISO, BSI, ANSI, WSSA)

### Synonyms

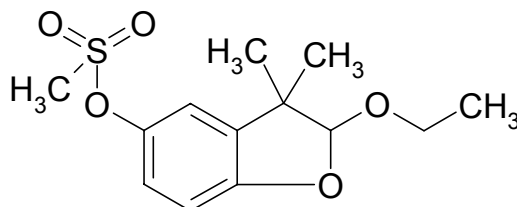
none

### Chemical names

**IUPAC** (±)-2-ethoxy-2,3-dihydro-3,3-dimethylbenzofuran-5-yl  
methanesulfonate

**CA** 5-benzofuranol, 2-ethoxy-2,3-dihydro-3,3-dimethylmethanesulfonate

### Structural formula



### Empirical formula

C<sub>13</sub>H<sub>18</sub>O<sub>5</sub>S

### Relative molecular mass

286.3

### CAS Registry number

26225-79-6

### CIPAC number

233

### Identity tests

HPLC retention time, IR, NMR

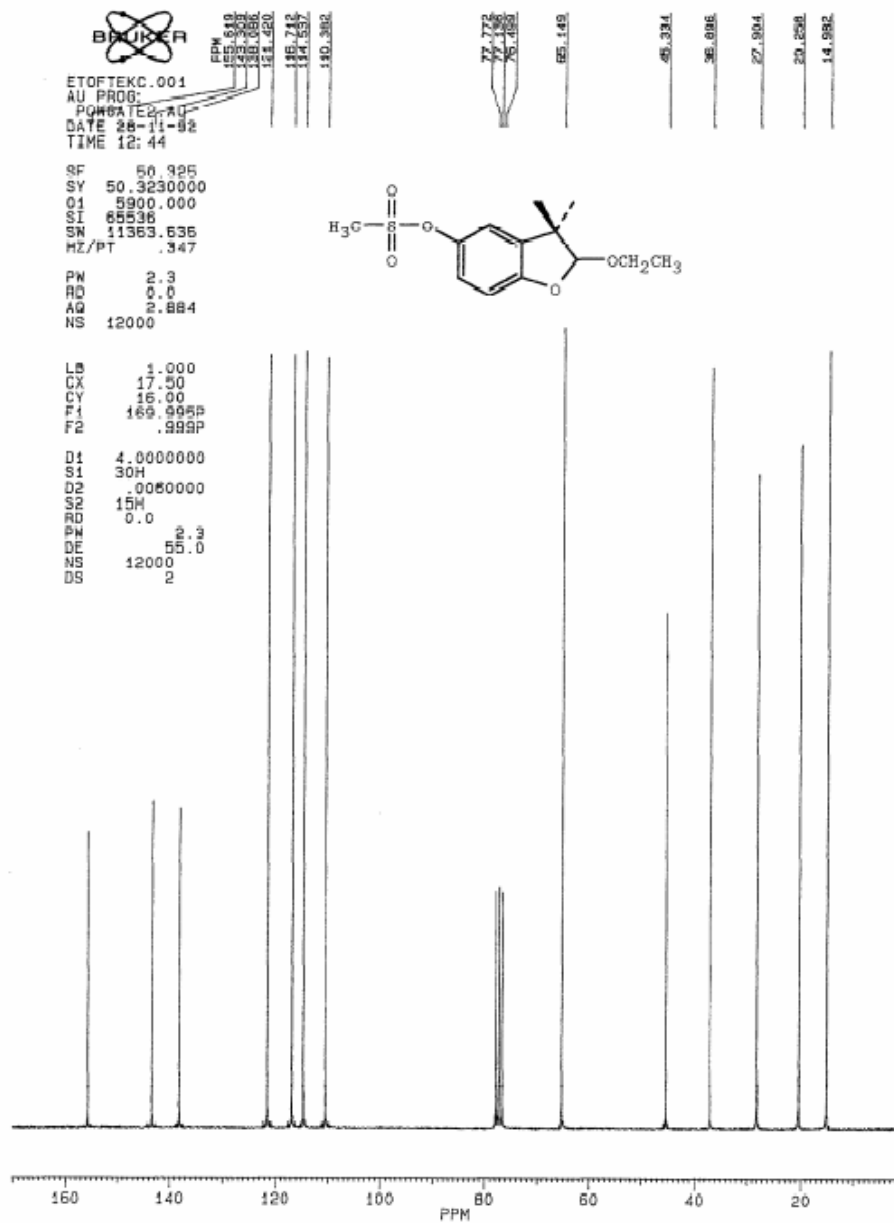


Figure 1. NMR spectrum of ethofumesate

## Physical and chemical properties

**Table 1. Physical and chemical properties of pure ethofumesate**

Parameter	Value(s) and conditions	Purity %	Method reference	Reference			
Vapour pressure	6.5 x 10 <sup>-5</sup> Pa at 25°C (by extrapolation)	99.9	gas saturation method with GLC detection	A82705			
Melting point	69.6 to 70.7°C	99.9	OECD 102 capillary method with photocell detection	A83412			
Decomposition temperature	Not determined	-	-	-			
Solubility in water	0.050 g/l at 25°C at pH 7.7	99.9	EEC A6 flask method	A82700			
	0.044 g/l at 20°C at pH 3 0.043 g/l at 20°C at pH 4 0.039 g/l at 20°C at pH 5	97	EEC A6 flask method	A87527			
	0.044 g/l at 20°C at pH 9 0.039 g/l at 20°C at pH 11	98	EEC A6 column elution method	A87528			
Octanol/water partition coefficient	log P K <sub>OW</sub> = 2.7 at 25°C at pH 6.8	99.9	EEC A8.3 Shake-flask method	A82703			
Hydrolysis characteristics	Half-life = 2050 d at 25°C at pH 4.97 Half-life = 940 d at 35°C at pH 4.97 No degradation at 25°C and 35°C at pH 6.99 or 9.23 (36 d)	radio-labelled compound	Based on US EPA guidelines working group draft 4/22/77	A83306			
Photolysis characteristics	In water (artificial light), half-life extrapolated to 8 to 13 d for a 12 h irradiation per day. Estimated half-lives (d) at the following latitudes and seasons were:			99.9	EPA Guideline, Subdivision N - Chemistry: Environmental Fate NTIS PB83-153973 EPA software: GCSOLAR	A83339, A83340	
		latitude 20°	latitude 40°				latitude 60°
	spring	40.9	59.6				120.0
summer	36.7	43.0	61.9				
Dissociation characteristics	Does not dissociate	-	-	-			

**Table 2. Chemical composition and properties of technical ethofumesate (TC)**

Manufacturing process, maximum limits for impurities $\geq 1$ g/kg, 5 batch analysis data	Confidential information supplied and held on file by WHO and FAO. Mass balances were 98.9–99.5% and no unidentified impurities were reported.
Declared minimum ethofumesate content	960 g/kg
Relevant impurities $\geq 1$ g/kg and maximum limits for them	Water, 5 g/kg.
Relevant impurities $< 1$ g/kg and maximum limits for them:	None <sup>1</sup> .
Stabilizers or other additives and maximum limits for them:	None.
Melting temperature range	47.6–69.0°C

### Background information on toxicology/ecotoxicology

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Ethofumesate has not been evaluated by the FAO/WHO JMPR or IPCS.

The European Commission's Standing Committee on the Food Chain and Animal Health established an ADI of 0-0.07 mg/kg/day, on 26 February 2002 (EU 2002).

The WHO classification of ethofumesate is class U, unlikely to present acute hazard in normal use (WHO 2002).

### Formulations

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The main formulation types available are EC, SC, SE and OD, for use in agriculture. These formulations are registered and sold in many countries throughout the world. Ethofumesate may be co-formulated with phenmedipham, bromoxynil, ioxynil, desmedipham or metamitron.

### Methods of analysis and testing

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The analytical method for ethofumesate (including identity tests) is CIPAC method 233/TM/C (CIPAC J), which encompasses TC, EC and SC. Extension of the analytical method to SE is also a full CIPAC method (CIPAC L). Ethofumesate is determined by reversed phase high performance liquid chromatography and quantified using ethyl benzoate as an internal standard. Extension of the method to analysis of OD has not yet been validated through CIPAC. Identification is by HPLC retention time and IR and NMR spectra.

Analytical methods for determination of impurities were based on HPLC, with UV detection and external standardization, and GC-FID using a semi-polar stationary phase and internal standardization. EMS and iBMS, proposed as relevant impurities were determined by a GC-MS/SIM method, with a limit of quantification of 0.1 mg/kg

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<sup>1</sup> There are no relevant impurities to be controlled in products of Bayer CropScience. However, ethyl methane sulfonate and/or iso-butyl methane sulfonate can occur as a result of certain manufacturing processes. If these impurities could occur at  $\geq 0.1$  mg/kg (relative to ethofumesate) in the products of other manufacturers, they would be designated as relevant impurities.



of ethofumesate. Peer validation data in support of the GC-MS/SIM method were provided to FAO.

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

### **Physical properties**

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The physical properties, the methods for testing them and the limits proposed for the EC, SC, SE and OD formulations complied with the requirements of the Manual (FAO/WHO, 2002).

### **Containers and packaging**

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No special requirements for containers and packaging have been identified.

### **Expression of the active ingredient**

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The active ingredient is expressed as ethofumesate, in g/kg or g/l at  $20 \pm 2^\circ\text{C}$ .

## **ANNEX 1**

### **HAZARD SUMMARY PROVIDED BY THE PROPOSER**

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

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

Species	Test	Purity %	Duration and conditions or guideline adopted	Results	Reference
Rat (m,f)	oral	96.3 – 99.5*	Dosed by gavage at 5000 mg/kg, observed 14 d	LD <sub>50</sub> >5000 mg/kg bw	A87559, A83223
Mouse (m,f)	oral	96.3 – 99.5*	Dosed by gavage at 5000 mg/kg, observed 14 d	LD <sub>50</sub> >5000 mg/kg bw	A87560
Rat (m,f)	dermal	96.3 – 99.5*	24 h semi-occluded exposure at 2000 mg/kg, observed 14 d	LD <sub>50</sub> >2000 mg/kg bw	A87561, A83224
Rabbit (m,f)	dermal	98	24 h occluded exposure at 2000 and 20050 mg/kg, observed 14 d	LD <sub>50</sub> >20050 mg/kg bw	A83173
Rat (m,f)	inhalation	96.3	4-h nose only exposure, observed 14 d	LC <sub>50</sub> >3.97 mg/l	A87562, A83217
Rabbit, New Zealand White	skin irritation	96.3 – 99.5*	4-h semi-occluded exposure to intact skin	Non-irritant	A87563, A83207
Rabbit, New Zealand White	eye irritation	96.3 – 99.5*	Eyes evaluated at 1, 24, 48, 72 and 96 h post-exposure.	Mild conjunctival irritation but classification not triggered	A87564, A83208
Guinea pig, Dunkin/Hartley	skin sensitization	96.3 – 99.5*	Magnusson and Kligman assay.	Negative	A87565

\* Purity was explicitly stated in these studies but the range of purity in batches of ethofumesate used in all toxicology studies performed during this period is shown.

Ethofumesate was of very low acute toxicity via the oral, dermal and inhalation route. No evidence of irritancy to the skin and only mild conjunctival effects in the eye, which did not trigger classification. No evidence of skin sensitization in a Magnusson and Kligman assay.

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

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Rat (m,f)	Dietary study	99.5	90 d, doses 0, 300, 3000, 30000 ppm	No critical effects but liver and kidney identified as target organs. NOAEL = 3000 ppm equivalent to 190 mg/kg/day (m) 230 mg/kg/day (f) LOEL = 30000 ppm equivalent to 1900 mg/kg/day (m) 2309 mg/kg/day (f)	A83225 A89580
Mouse	Dietary study	97	90 d, doses 0, 300, 3000, 10000 ppm	No critical effects. NOAEL = 10000 ppm equivalent to approximately 1200 mg/kg/day.	A89579

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

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Dog (m,f)	Gavage study	97	90 d, doses 0, 250, 750, 1500 mg/kg/day.	No critical effects. NOAEL = 250 mg/kg/day (m,f) LOEL = 750 mg/kg/day.	A87568
Rabbit, New Zealand White (m,f)	Dermal study	96	6 h daily exposure for 21 d consecutive, doses 0, 100, 300, 1000 mg/kg/day.	NOAEL = 1000 mg/kg/day.	A83209
Rat (m,f)	Feeding study	97	1 year, doses 0, 2000, 7000, 20000 ppm	No critical effects. Slight reductions in weight gain and food intake. Increases in liver weight and periportal hepatocyte enlargement showed liver is target organ. NOAEL = 2000 ppm equivalent to 135 mg/kg/day (m) 164 mg/kg/day (f) LOEL = 7000 ppm equivalent to c. 470mg/kg/day (m) c. 630 mg/kg/day (f)	A89582
Rat	Feeding study	97	2 year, doses 0, 2000, 7000, 20000 ppm	Not carcinogenic. Slight reductions in weight gain and food intake. Increases in liver weight and centrilobular hepatocyte hypertrophy showed liver is target organ. NOAEL = 2000 ppm equivalent to 100 mg/kg/day	A89583, A83155
Hamster (m,f)	Oncogenicity study	97.4	19/22 month feeding, doses 0, 80, 400, 2000 ppm.	Not carcinogenic, no critical effects. NOAEL = 400 ppm equivalent to 26 mg/kg/day (m) 28 mg/kg/day (f)	A83178
Dog	Dietary feeding study	97.8	24 month, doses 0, 800, 4000, 20000 ppm	No critical effects observed. Slight reductions in red cell count and haemoglobin and increases in alkaline phosphatase, AST and liver weight were observed at the high dose level. NOAEL = [ 4000 ppm] equivalent to 118 mg/kg/day for males and 109mg/kg/day for females LOEL = [ 20000 ppm ] equivalent to 632mg/kg/day for males and 619 mg/kg/day.	A83176
Rat (m,f)	Multi-generation study	>97	2-generation, doses 0, 200, 1000, 5000 ppm	No effects on reproduction or fertility. NOAEL = 5000 ppm equivalent to c. 397 mg/kg/day (m) c. 454 mg/kg/day (f)	A87579, A83174

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

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Reference
Rat	Teratology study	>97	Doses 0, 1000, 2000, 4000 mg/kg/day.	No embryotoxicity or developmental toxicity. NOAEL = 4000mg/kg/day (dams and foetuses)	A87575
Rat	Teratology study	97	Doses 0, 10, 100, 1000 mg/kg/day.	No embryotoxicity or developmental toxicity. NOAEL = 1000mg/kg/day (dams and foetuses)	A83205
Rabbit	Teratology study	>97	Doses 0, 300, 600, 1200 mg/kg/day	No embryotoxicity or developmental toxicity. Non-specific maternal reduced weight gain at 1200 mg/kg/day. NOAEL = 1200mg/kg/day (foetuses) 600 mg/kg/day (dams)	A87577

Short-term repeat dose oral studies in rat, mouse and dog showed that ethofumesate was very well tolerated and that the principle target organs were the liver and kidney. In these sub-chronic studies, no effect levels of c. 200 mg/kg/day, c. 1200 mg/kg/day and 250 mg/kg/day were established in the rat, mouse and dog, respectively. No effects whatsoever were seen in a sub-acute dermal toxicity in the rabbit at the dose limit of 1000 mg/kg/day. No evidence of oncogenicity was observed in carcinogenicity studies in the rat and hamster. Chronic toxicity studies performed on the rat and dog confirmed that the material well tolerated. In these studies the liver was the major target organ and no effect levels were established at 135 (m) and 164 (f) mg/kg/day in rat and 118 (m) and 109 (f) mg/kg/day in dog. Ethofumesate did not affect reproduction in a multi-generation study in the rat. No evidence of embryotoxicity or developmental toxicity was seen in either the rat or the rabbit.

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

Species	Test	Purity %	Conditions and doses	Result	Reference
<i>Salmonella typhimurium</i> , strains TA98, TA100, TA1535, TA1537 and TA 1538	Bacterial reverse mutation assay, <i>in vitro</i> .	97.2	With and without metabolic activation, ≤5000 µg/plate	Negative	A83222, A87570
Human lymphocytes	<i>In vitro</i> chromosome aberration test	96.3	With and without metabolic activation, 11, 55 and 110 µg/ml.	Negative	A83192
Mouse L5178Y lymphoma cells	<i>In vitro</i> gene cell mutation assay	96.3	With and without metabolic activation ≤250 µg/ml.	Negative	A83191
Rat (Fisher), cultured hepatocytes	<i>In vitro</i> DNA repair assay	96.3	≤200 µg/ml	Negative	A83194
Mouse	<i>In vivo</i> micronucleus formation assay	96.3	8100 mg/kg	Negative	A83189

In *in vitro* and *in vivo* mutagenicity studies, no evidence of genotoxicity was observed.

**Table D. Ecotoxicology profile of ethofumesate technical material**

Species	Test	Purity %	Duration and conditions	Results	Reference
<i>Anas platyrhynchos</i> (mallard duck)	Acute oral toxicity	97, n.s.	2 studies, TC suspended in corn oil up to 2000 and 3552 mg/kg bw.	LD <sub>50</sub> >2000 mg/kg bw (study 1) 3552 mg/kg bw (study 2)	A87610, A83331
<i>Colinus virginianus</i> (bobwhite quail)	Acute oral toxicity	97, n.s.	2 studies, TC suspended in corn oil up to 2000 and 8743 mg/kg bw.	LD <sub>50</sub> >2000 mg/kg bw (study 1) 8743 mg/kg bw (study 2)	A87612, A83330
<i>Anas platyrhynchos</i> (mallard duck)	Dietary toxicity	97.6, 97	Two 8-day (5-day exposure, 3-day observation period) studies, TC doses up to 5200 ppm diet.	LC <sub>50</sub> >1082 mg/kg bw/d (study 1) 1345 mg/kg bw/d (study 2)	A83367, A87611
<i>Colinus virginianus</i> (bobwhite quail)	Dietary toxicity	98, 97	Two 8-day (5-day exposure, 3-day observation period) studies, TC doses up to 5200 ppm diet.	LC <sub>50</sub> >839 mg/kg bw/d (study 1) 1050 mg/kg bw/d (study 2)	A83369, A87613
<i>Oncorhynchus mykiss</i> (rainbow trout)	Acute toxicity	98.1, >97	96 h, static 96 h, semi-static	LC <sub>50</sub> = 20.2 mg/l LC <sub>50</sub> = 11.91 mg/l	A83375, A87614
<i>Lepomis macrochirus</i> (bluegill sunfish)	Acute toxicity	>97, 97.8	96 h, semi-static 96 h, semi-static	LC <sub>50</sub> = 21.2 mg/l LC <sub>50</sub> = 12.37 mg/l	A87615, A83373
<i>Cyprinus carpio</i> (mirror carp)	Acute toxicity	99.9	96 h, semi-static	LC <sub>50</sub> = 10.92 mg/l <sup>1</sup>	A83349
<i>Pimephales promelas</i> (fathead minnow)	Chronic toxicity	97	28 d, early life stage, embryos incubated with up to 23.2 mg/l TC	LC <sub>50</sub> = 16.3 mg/l	A83372
<i>Oncorhynchus mykiss</i> (rainbow trout)	Chronic toxicity, juvenile growth	97	21 d, flow-through 21 d, semi-static	LC <sub>50</sub> >20 mg/l LC <sub>50</sub> = 21.56 mg/l	A87616
<i>Salmo gairdneri</i>	Chronic toxicity	99.9	21 d, semi-static	LC <sub>50</sub> = 31.1 mg/l	A83355
<i>Lepomis macrochirus</i> (bluegill sunfish)	Bio-accumulation	>99, 97.5	two 28 d studies, exposure to 0124 mg/l or 0.56 mg/l followed by 14 d depuration	Bioaccumulation occurred but 99% elimination within 3 d depuration	A87617, A83371
<i>Daphnia magna</i> (water flea)	Acute toxicity	97.5, >97	Two 48-h static studies with observation at 24 and/or 48 h	EC <sub>50</sub> = 13.52 mg/l (48 h study 1); EC <sub>50</sub> = 34 mg/l (24 h study 2); EC <sub>50</sub> = 22 mg/l (48 h study 2)	A83370, A87618

<sup>1</sup> Considered less reliable than rainbow trout and bluegill sunfish due to solubility issues.  
n.s. = not stated in report.

**Table D. Ecotoxicology profile of ethofumesate technical material**

Species	Test	Purity %	Duration and conditions	Results	Reference
<i>Daphnia magna</i> (water flea)	Chronic toxicity	97, 99.9	Study 1, 21-d exposure, semi-static Study 2, 21-d exposure, flow through	LC <sub>50</sub> (survival) = 13.5 mg/l (study 1) 4 mg/l (study 2) EC <sub>50</sub> (reproduction) = 1.2 mg/l (study 1) 1.35 mg/l (study 2)	A87619, A83345
<i>Scenedesmus</i> or <i>Desmodesmus subspicatus</i> (green alga)	Effect on growth	97, 99.9	Study 1, 72-h exposure, static Study 2, 93-h exposure, static	ErC <sub>50</sub> = 9 mg/l (0-24 h study 1) ErC <sub>50</sub> = 1.8 mg/l (93 h study 2) EbC <sub>50</sub> = 3.9 mg/l (study 1) EbC <sub>50</sub> = 0.06 mg/l (study 2) <sup>1</sup>	A87620, A83343
<i>Apis mellifera</i> (honey bee)	Acute oral and contact toxicity	99.9, 97	Dosed with TC, observed 48 h	LD <sub>50</sub> >100 µg/bee	A83374, A87621
<i>Aleochara bilineata</i> (staphylinid beetle)	Acute toxicity	f.p.	Exposure to fresh/dried residues of Tramat/Nortron 50SC formulations applied to sand (equivalent to 1252.5 g/ha ethofumesate), 4 d	No effect on survival or reproduction	A83379
<i>Poecilus cupreus</i> (carabid beetle)	Acute toxicity	f.p.	Exposure to fresh/dried residues of Tramat/Nortron 50SC formulations applied to sand (equivalent to 2000 g/ha ethofumesate), 14 d	No effect on survival	A83354
<i>Chrysoperla carnea</i> (lacewing)	Acute toxicity	f.p.	Exposure to dried residues of Tramat/Nortron 50SC formulations applied to glass plates (equivalent to 2000 g/ha ethofumesate) until pupation, assessment of egg production from emerged adults over 4 weeks	No effect on larval survival or on subsequent reproduction	A83377
<i>Eisenia foetida</i> (earthworm)	Acute toxicity	97	Two 14-d exposure studies, artificial soil treated with TC up to 1000 mg/kg soil, 14 d	LC <sub>50</sub> = 134 mg/kg (study 1) LC <sub>50</sub> = 383 mg/kg (study 2)	A87622
Soil micro-organisms	Soil respiration	>97, 97.7	Study 1, 28-d, loamy sand and sandy clay soils treated with TC at 1.18 and 5.98 mg/kg soil, equivalent to 900 and 4500 g/ha. Study 2, 63-d, sandy and clay soils treated with TC at 1.87 and 9.35 mg/kg soil, equivalent to 1400 and 7000 g/ha.	No significant effect on soil microflora respiration	A87660, A83392

<sup>1</sup> Study 2 was considered inconsistent. The risk assessment and EC classification for toxicity were based on the 72-h exposure study.  
f.p. = formulated product, and purity not determined.

**Table D. Ecotoxicology profile of ethofumesate technical material**

Species	Test	Purity %	Duration and conditions	Results	Reference
Soil micro-organisms	Soil ammonification and nitrification	>98	Soils amended with lucerne meal, incubated 6 weeks with TC at 0.3 and 3.0 mg/kg soil, equivalent to 230 and 2300 g/ha	No significant effect on soil ammonification and nitrification capacity of soil micro-organisms	A87623
Soil micro-organisms	Soil nitrification	f.p.	Sandy loam soil treated with 2 and 40 kg ethofumesate/ha and assessed for soil nitrification and respiration, fungal content and enzymatic activities	Minor impact on microbial populations and enzymatic activities, some slowing of nitrification, not severe or irreversible	A83282
Activated sludge		n.s., n.s.	Two laboratory activated sludge studies. Study 1, continuous or twice weekly dosing with 100mg/l ethofumesate. Study 2 with a 30-d acclimated and unexposed activated sludge subsequently treated with 100 mg/l ethofumesate for 48 h	Study 1, no permanent adverse effects on performance or health of activated sludge process. Study 2, no inhibition of the activated sludge.	A83275, A83276

n.s. = not stated in report.

f.p. = formulated product and purity not determined.

No treatment-related effects to either bobwhite quail or mallard duck in acute oral and short-term dietary studies, at rates well in excess of regulatory limits. It is therefore of low toxicity to avian species and no avian reproduction study was conducted.

Low toxicity to fish, which is not increased by prolonged exposure. There is no risk of bioaccumulation of ethofumesate in fish. Low toxicity to *Daphnia magna*. Ethofumesate is relatively toxic to the green alga, *S. or D. subspicatus*, and should be classified as toxic to aquatic organisms.

Ethofumesate is of low risk to honeybees, harmless to soil and foliage dwelling beneficial arthropods, and of low toxicity to earthworms. It did not significantly affect soil micro-organism respiration when applied at field rates up to 7000 g/ha, while the results of nitrification experiments indicated that only minor, short-term inhibition occurred at rates of up to 40 kg ethofumesate/ha. Ethofumesate is unlikely to affect the functioning of sewage treatment plants.



## ANNEX 2. REFERENCES

Bayer CropScience document No. or other reference	Year and title or publication details
A82700	1988. Ethofumesate: Solubility in water at 25C.
A82703	1990. Ethofumesate: Determination of the partition coefficient between octanol and water at 25C.
A82705	1988. Ethofumesate: determination of the vapour pressure of ethofumesate
A83155	1976. The effects of the dietary administration of NC 8438 to male and female rats for two years.
A83173	1979. Ethofumesate technical CR 4805/4 : Acute dermal toxicity study in rabbits.
A83174	1980. Technical NC 8438 : Multigeneration study in the rat.
A83176	1980. Technical NC 8438 toxicity study in beagle dogs (final report : dietary intake for 104 weeks).
A83178	1980. A carcinogenicity study of NC 8438 in hamsters.
A83189	1985. Technical ethofumesate : Mouse micronucleus test.
A83191	1986. Technical ethofumesate : Mouse lymphoma (6TG) fluctuation assay.
A83192	1986. Technical ethofumesate : Metaphase chromosome analysis of human lymphocytes cultured in vitro.
A83194	1988. Technical ethofumesate : Assessment of unscheduled DNA synthesis using rat hepatocyte cultures.
A83205	1991. Technical ethofumesate oral teratology (developmental toxicity) study in the rat.
A83207	1991. Technical Ethofumesate: Rabbit skin irritancy study.
A83208	1991. Technical ethofumesate: Rabbit eye irritancy study.
A83209	1991. Technical ethofumesate : Rabbit twenty-one day dermal toxicity study.
A83217	1988. Ethofumesate technical : Acute inhalation toxicity study four hour exposure in the rat.
A83222	1994. Ethofumesate : Bacterial mutation assay.
A83223	1988. Technical ethofumesate powder: Acute oral toxicity (limit test) in the rat.
A83224	1988. Tech. Ethofumesate powder: Acute dermal : toxicity (limit test) in the rat.
A83225	1989. Ethofumesate technical : Ninety day oral (dietary administration) toxicity study in the rat.
A83275	1979. Effects of technical ethofumesate on the performance of the activated sludge process.
A83276	1978. Investigation of the metabolism of the compound ethofumesate (NC 8438, Nortron) by activated sludge.
A83282	Voets, J. P. <i>et al.</i> , 1977. The influence of pyrazon, ethofumesate and metamitron on the soil microbiota. <i>Acta Phytopath. Acad Scient. Hung.</i> <b>12</b> , (1-2), 31-39.
A83306	1978. The hydrolysis of ethofumesate under acidic neutral and basic conditions.
A83330	1977. The acute oral toxicity (LD50) of NC 8438 to the bobwhite quail.
A83331	1977. The acute oral toxicity (LD50) of NC 8438 to the mallard duck.
A83339	1989. The photolysis of ethofumesate (Schering code no. ZK 49 913) in aqueous solution.
A83340	1989. The photolysis of ethofumesate (Schering code no. ZK 49 913) in aqueous solution.
A83343	1989. A study of the toxicity to algae of ethofumesate technical.
A83345	1989. The chronic toxicity of ethofumesate to <i>Daphnia magna</i> .
A83349	1989. Technical ethofumesate – Determination of acute toxicity (LC50) to mirror carp (96 hours, semi static) and the analysis of ethofumesate in water samples.

Bayer CropScience document No. or other reference	Year and title or publication details
A83354	1990. A study of the acute toxicity of Trammat 500 (Nortron 50SC) to the carabid <i>Poecilus cupreus</i> .
A83355	1990. A study of the prolonged toxicity to fish ( <i>Salmo gairdneri</i> ) of ethofumesate technical.
A83367	1991. Technical ethofumesate : Subacute dietary toxicity (LC50) to mallard duck.
A83369	1991. Technical ethofumesate : Subacute dietary toxicity (LC50) to bobwhite quail.
A83370	1991. Determination of the acute toxicity of [14C]- ethofumesate to <i>Daphnia magna</i> .
A83371	1991. Determination of the accumulation and elimination of [14C]-ethofumesate in bluegill sunfish ( <i>Lepomis macrochirus</i> ).
A83372	1991. Ethofumesate – Fathead minnow ( <i>Pimephales promelas</i> ) early life stage toxicity test.
A83373	1991. The acute toxicity of [14C]-ethofumesate to bluegill sunfish ( <i>Lepomis macrochirus</i> ) under semi static conditions.
A83374	1991. The acute oral and topical toxicities of ethofumesate to worker honeybees ( <i>Apis mellifera</i> L.).
A83375	1991. The acute toxicity of [14C]-ethofumesate to rainbow trout ( <i>Oncorhynchus mykiss</i> ) under static conditions.
A83377	1990. Side effects of Trammat 500 on the lacewing <i>Chrysoperla carnea</i> Steph in the laboratory.
A83379	1991. An evaluation of the side effects of Trammat 500 SC on the staphylinid beetle ( <i>Aleochara bilineata</i> ).
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