Food and Agriculture Organization
of the United Nations

FAO SPECIFICATIONS AND EVALUATIONS

FOR AGRICULTURAL PESTICIDES

ETHEPHON

(2-chloroethyl)phosphonic acid

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ETHEPHON

DISCLAIMER[1]

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

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

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

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[1] This disclaimer applies to all specifications published by FAO.

INTRODUCTION

FAO establishes and publishes specifications* for technical material and related formulations of agricultural pesticides, with the objective that these specifications may be used to provide an international point of reference against which products can be judged either for regulatory purposes or in commercial dealings.

From 1999 onward, the development of FAO specifications follows the **New Procedure**, described first in the 5th edition of the "Manual on the development and use of FAO specifications for plant protection products" and later in the 1st edition of "Manual for Development and Use of FAO and WHO Specifications for Pesticides" (2002) - currently available as the 2nd edition of the "Manual on development and use of FAO and WHO specifications for chemical pesticides (2022)"-, which is available only on the internet through the FAO and WHO web sites.

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 JMPM, rather than the JMPS.]

FAO Specifications now only apply to products for which the technical materials have been evaluated. Consequently, from the year 1999 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 pesticide in accordance with chapters 4 to 8 of the "Manual on development and use of FAO and WHO specifications for chemical pesticides".

Part Two: The Evaluation Report(s) of the pesticide, reflecting the evaluation of the data package carried out by FAO and the JMPS. The data are provided by the manufacturer(s) according to the requirements of chapter 3 of the "FAO/WHO Manual on Pesticide Specifications" and supported by other information sources. The Evaluation Report includes the name(s) of the manufacturer(s) whose technical material has been evaluated. Evaluation reports on specifications developed subsequently to the original set of specifications are added in a chronological order to this report.

FAO specifications developed under the **New Procedure** do not necessarily apply to nominally similar products of other manufacturer(s), nor to those where the active ingredient is produced by other routes of manufacture. FAO has the possibility to extend the scope of the specifications to similar products but only when the JMPS has been satisfied that the additional products are equivalent to that which formed the basis of the reference specification.

Specifications bear the date (month and year) of publication of the current version. 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 (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/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/pesticide-specifications-list/en/

PART ONE

SPECIFICATIONS

ETHEPHON

ETHEPHON

INFORMATION

ISO common name

There is no ISO common name for this substance; the name “ethephon” is approved by the American National Standards Institute (ANSI).

Synonyms

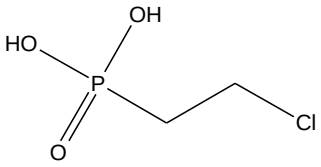
None

Chemical names

IUPAC (2-chloroethyl)phosphonic acid

CAS (*P*)-(2-chloroethyl)phosphonic acid

Structural formula



Molecular formula

$C_2H_6ClO_3P$

Relative molecular mass

144.5

CAS Registry number

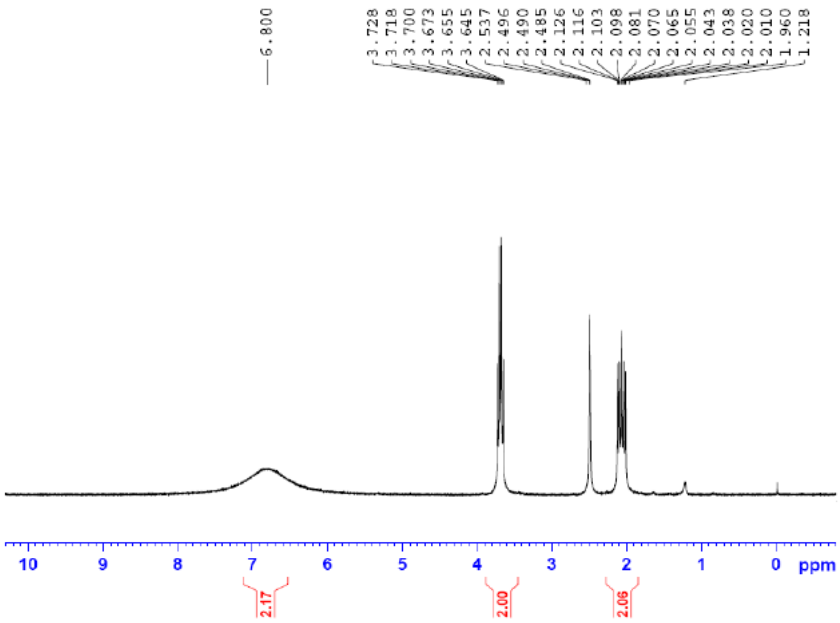
16672-87-0

CIPAC number

373

Identity tests

Retention time in ion chromatography, ^{1}H-NMR



ETHEPHON TECHNICAL MATERIAL

FAO Specification 373 / TC (June 2023*)

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 (373/2022). 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 specification. The specification may not be appropriate for the products of other manufacturers. The evaluation report (373/2022) as PART TWO forms an integral part of this publication.

1 Description

The material shall consist of ethephon together with related manufacturing impurities, in the form of grayish white colored waxy solid, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (373/TC/M2/2, CIPAC/5315) (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 **Ethephon content** (373/TC/M2/3, CIPAC/5315) (Note 1)

The ethephon content shall be declared (not less than 930 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

3 **Relevant impurities** (Note 2)

Note 1 The ion-chromatographic method (CIPAC/5315) for the determination of ethephon in TC, TK and SL formulations was accepted as provisional CIPAC method (ISBN 978-1-911009-63-4). Prior to its publication in a next Handbook, the method is available through the CIPAC pre-publishment scheme from https://www.cipac.org/index.php/m-p/pre-published-methods

Note 2 There are not relevant impurities that have to be controlled in the products of the manufacturer identified in the evaluation report 373/2022. However, residues of 1,2-dichloroethane may occur as a result of certain production processes. If this impurity would occur at > 0.2 g/kg, this compound would be considered as a relevant impurity and a clause would be required to limit its concentration.

* 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/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/pesticide-specifications-list/en/

ETHEPHON TECHNICAL CONCENTRATE

FAO Specification 373 / TK (June 2023*)

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 (373 /2022). It should be applicable to relevant products of this manufacturer, and those of any other formulators who use only TC from the evaluated source. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers who use TC from other sources. The evaluation report (373/2022), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of ethephon together with related manufacturing impurities and shall be a colorless to tan liquid free from visible extraneous matter and added modifying agents except for the diluent.

2 Active ingredient

2.1 **Identity tests** (373/TK/M2/2-, CIPAC/5315) (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 **Ethephon content** (373/TK/M2/3, CIPAC/5315) (Note 1)

The ethephon content shall be declared (above 500 g/kg or 500 g/l at 20 ± 2°C) and, when determined, the average measured content shall not differ from that declared by more than ± 25 g/kg of the declared content.

3 Relevant impurities (Note 2)

4 Physical properties

4.1 **pH range** (MT 75.3, CIPAC Handbook J, p.131, 2000)

pH range (1 % aqueous dilution): 1.5 to 2.0.

Note 1 The ion-chromatographic method (CIPAC/5315) for the determination of ethephon in TC, TK and SL formulations was accepted as provisional CIPAC method (ISBN 978-1-911009-63-4). Prior to its publication in a next Handbook, the method is available through the CIPAC pre-publishment scheme from https://www.cipac.org/index.php/m-p/pre-published-methods

* 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/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/pesticide-specifications-list/en/

Note 2 There are not relevant impurities that have to be controlled in the products of the manufacturer identified in the evaluation report 373/2022. However, residues of 1,2-dichloroethane may occur as a result of certain production processes. If this impurity would occur at > 0.02 % (of the ethephon content), this compound would be considered as a relevant impurity and a clause would be required to limit its concentration.

ETHEPHON SOLUBLE CONCENTRATE

FAO Specification 373 / SL (June 2023*)

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 (373 /2022). It should be applicable to relevant products of this manufacturer, and those of any other formulators who use only TC from the evaluated source. The specification is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers who use TC from other sources. The evaluation report (373/2022), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of technical ethephon, complying with the requirements of FAO specification 373/TC, dissolved in suitable solvents, together with any other necessary formulants. It shall be in the form of a clear or opalescent colorless to tan liquid, free from visible suspended matter and sediment, to be applied as a true solution of the active ingredient in water.

2 Active ingredient

2.1 **Identity tests** (373/SL/M2/2, CIPAC/5315) (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 **Ethephon content** (373/SL/M2/3, CIPAC/5315) (Note 1)

The ethephon content shall be declared (g/kg or g/l at 20 ± 2ºC, 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 ± 2°C	Tolerance
above 100 up to 250	± 6% of the declared content
above 250 up to 500	± 5% of the declared content
above 500	± 25 g/kg or g/l
Note: In each range the upper limit is included	

3 Relevant impurities (Note 3)

* 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/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/pesticide-specifications-list/en/

4 Physical properties

4.1 **pH range** (MT 75.3, CIPAC Handbook J, p.131, 2000)

pH range (1 % aqueous dilution): 1.5 to 3.0.

4.2 **Dilution stability** (MT 41.1, CIPAC Handbook O, p.174, 2017)

The formulation, following dilution (Note 4) with CIPAC standard water D and standing at 30 ± 2°C for 24 h, shall give a clear or opalescent solution, free from more than a trace of sediment and visible solid particles. Any visible sediment or particles produced shall pass through a 75 µm test sieve.

4.3 **Persistent foam** (MT 47.3, CIPAC Handbook O, p.177, 2017) (Note 5)

Maximum: 25 ml after 1 min.

5 Storage stability

5.1 **Stability at 0°C** (MT 39.3, CIPAC Handbook J, p.126, 2000)

After storage at 0 ± 2°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 46.4, CIPAC Handbook P, p.232, 2021)

After storage 54 ± 2°C for 14 days, the determined average active ingredient content must not be lower than 95% relative to the determined average content found before storage (Note 6) and the formulation shall continue to comply with the clauses for:

- pH range (4.1)
- dilution stability (4.2)

Note 1 The ion-chromatographic method (CIPAC/5315) for the determination of ethephon in TC, TK and SL formulations was accepted as provisional CIPAC method (ISBN 978-1-911009-63-4). Prior to its publication in a next Handbook, the method is available through the CIPAC pre-publishment scheme from https://www.cipac.org/index.php/m-p/pre-published-methods

Note 2 If the buyer requires both g/kg and g/l at 20°C, then in case of dispute the analytical results shall be calculated as g/kg.

Note 3 There are not relevant impurities that have to be controlled in the products of the manufacturer identified in the evaluation report 373/2022. However, residues of 1,2-dichloroethane may occur as a result of certain production processes. If this impurity would occur at > 0.02 % (of the ethephon content), this compound would be considered as a relevant impurity and a clause would be required to limit its concentration.

Note 4 The concentration used in the test should correspond to the highest rate of use recommended by the supplier provided it is within the scope of the method.

Note 5 The mass of sample to be used in the test should be at the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at 25 ± 5°C.

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

PART TWO

EVALUATION REPORT

ETHEPHON

ETHEPHON

FAO/WHO EVALUATION REPORT 373/2022

Recommendations

The Meeting recommended the following:

(i) The specifications for ethephon TC, TK and SL, proposed by Shaoxing Eastlake High-Tech Co., Ltd. and converted from the old procedure specifications and amended, should be adopted by FAO.

(ii) The FAO specifications for ethephon TC, TK and SL developed under the old procedure should be withdrawn.

Appraisal

Ethephon is a systemic plant growth regulator. The compound is not under patent.

Ethephon was several times evaluated for toxicology by the FAO/WHO JMPR in 1977, 1978, 1993, 1995, 1997, 2002 and re-evaluated in 2015 as part of the periodic review programme of the Codex Committee on Pesticide Residues [JMPR, 2015 a].

The old procedure FAO specifications for the technical material (373/TC/S/F (2000)), technical concentrate (373/TK/S/F (2000)) and soluble concentrates (373/TC/S/F (2000)) were published in 2000 [AGP:CP/367].

The data for ethephon were evaluated in support of a conversion of the specifications developed under the old procedure into the corresponding new ones, based on the draft specifications and the supporting data provided by Shaoxing Eastlake High-Tech Co., Ltd (Shaoxing Eastlake).

The data submitted were mainly in accordance with the requirements of the Manual on the development and use of FAO and WHO specifications for chemical pesticides (second edition) and supported the proposed specifications [FAO/WHO Manual].

Ethephon is currently registered and sold in many countries throughout the world.

A statement was provided by the Institute for the Control of Agrochemicals, Ministry of Agriculture and Rural Affairs (ICAMA), China that the confidential data on the manufacturing process and declaration of composition submitted to the FAO were the same as those submitted to the national regulatory authorities [Chen].

Ethephon is a white crystalline powder (98.5 %) with a melting point of 72.0-73.6°C. There is no boiling point at atmospheric pressure, it decomposes at 250–400°C. The solubility in water is > 1000 g/l at pH < 0.2, 800 g/l at pH 4, at pH > 5 no solubility can be determined because of decomposition. It is readily soluble in a range of medium polarity organic solvents such as methanol (> 600 g/l), acetone (> 600 g/l) and acetonitrile (> 600 g/l). The *n*-octanol/water partition coefficient is in the range -0.63 to -1.81 in the pH range 2 to 10. The

vapour pressure is $<1.0\times10^{-3}$ Pa (from 18 to 80°C) Two dissociation constants in water are: $pK_1 = 2.82$ and $pK_2 = 7.21$ [JMPR, 2015 b].

The Meeting was provided with commercially confidential information on the manufacturing process and batch analysis data on all impurities present below or above 1 g/kg and their manufacturing limits in the TC. Mass balances were 98.04-98.22% in the 5-batch data. The intention of Shaoxing Eastlake was to apply for a FAO specification of minimum 930 g/kg, higher than the old procedure TC specification (minimum 910 g/kg).

In the submission the company considered, based on the old FAO specification, that MEPHA [2-chloroethyl hydrogen (2-chloroethyl)phosphonate] and 1,2-dichloroethane are relevant impurities in the TC and in addition insolubles in water are relevant in the TK. In the updated submission 1,2-dichloroethane was not considered relevant since its level in the TC product was below the LOD (0.087 g/kg) and Shaoxing Eastlake proposed a note to the specifications indicating that 1,2-dichloroethane could occur as a result of certain manufacturing processes.

1,2-dichloroethane is a carcinogen and hence a potential relevant impurity. ECHA classified 1,2-dichloroethane in Category 1B for carcinogenicity and a maximum acceptable limit based on UN GHS of 1 g/kg can be derived for 1,2-dichloroethane. However, there are published data on 1,2-dichloroethane permitting a more refined approach. The US EPA derived an oral slope factor of 9.1×10^{-2} per mg/kg-day (an oral slope factor is an estimate of the increased cancer risk from oral exposure to a dose of 1 mg/kg-day for a lifetime). Based on a cancer risk of 10^{-5} a health based guidance value of 0.0001 mg/kg bw/day can be derived for 1,2-dichloroethane. For ethephon, JMPR derived an acceptable daily intake and an acute reference dose of the same value, 0.05 mg/kg bw/day. According to Appendix H of the FAO/WHO Manual, a maximum acceptable value of 0.2 g/kg can be derived. It was proposed to set the limit for 1,2-dichloroethane in ethephon at 0.2 g/kg. Since 1,2-dichloroethane cannot be detected in the TC, it was agreed to include a note in the specifications that residues of 1,2-dichloroethane may occur as a result of certain production processes and if this impurity would occur at > 0.2 g/kg, this compound would be considered as a relevant impurity and a clause would be required to limit its concentration.

The Meeting re-considered the relevance of the impurity mono 2-chloroethyl ester, 2-chloroethyl phosphonic acid (MEPHA). The comparative (Q)SAR analysis with DEREK and SARAH with MEPHA and ethephon showed that all alerts fired by MEPHA were also fired by ethephon. On this basis, the Meeting considered MEPHA as non relevant.

Under the conditions of the test, in which ethephon TC was tested up to the recommended maximum test concentration for soluble non-cytotoxic substances, i.e., 5.0 mg mg/plate, ethephon TC was not mutagenic under the conditions of the test.

The acute toxicity data, the bacterial reverse mutation test and the repeated dose 28-day oral toxicity study in rodents were generated using the proposer's material. The repeated and chronic toxicity data, the chromosomal aberration and UDS *in vitro* data, as well as

ecotoxicity data were generated using material from sources other than the proposer. The purity of the test item used in these studies was 71.3%, much lower than the proposer's product (75% TK).

The active ingredient and its impurities were quantified using validated methods by high performance ion chromatography and gas-liquid chromatography, with LOQs from 0.27 to 13.11 g/kg for the impurities. The method used for the determination of the active ingredient in the 5-batch analysis was the ion-chromatographic method (CIPAC/5315) for the determination of ethephon in TC, TK and SL formulations, accepted as provisional CIPAC method. The identity of the active ingredient ethephon in the technical batches was confirmed by IC retention time and NMR.

The identity of all impurities was confirmed by retention time using certified reference standards. Residual water in the TC was analyzed by Karl-Fischer titration [CIPAC, F].

The proposed specifications for ethephon TC, TK and SL were broadly in accordance with the requirements of the FAO/WHO Manual, however the Meeting recommended to remove the clauses for material insoluble in water and water from the list of relevant impurities in the TK. Furthermore, a note concerning the possible content of the relevant impurity 1,2-dichloroethane was deemed to be necessary.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 373/2022

Uses

Ethephon is a plant growth regulator. It penetrates into the plant tissues, and is decomposed to ethylene, which affects the growth processes. It is used in agriculture and horticulture to promote pre-harvest ripening in apples, currants, blackberries, blueberries, cranberries, morello cherries, citrus fruit, figs, tomatoes, sugar beet and fodder beet seed crops, coffee, capsicums, etc.; to accelerate post-harvest ripening in bananas, mangoes and citrus fruit; to facilitate harvesting by loosening of the fruit in currants, gooseberries, cherries and apples; to increase flower bud development in young apple trees; to prevent lodging in cereals, maize and flax; to induce flowering of Bromeliads; to stimulate lateral branching in azaleas, geraniums and roses; to shorten the stem length in forced daffodils; to induce flowering and regulate ripening in pineapples; to accelerate boll opening in cotton; to modify sex expression in cucumbers and squash; to increase fruit setting and yield in cucumbers; to improve the sturdiness of onion seed crops; to hasten the yellowing of mature tobacco leaves; to stimulate latex flow in rubber trees, and resin flow in pine trees; to stimulate early uniform hull split in walnuts.

Identity of the active ingredient

ISO common name

There is no ISO common name for this substance; the name “ethephon” is approved by the American National Standards Institute (ANSI)

Synonyms

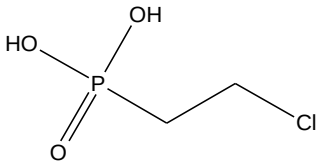
None

Chemical names

IUPAC (2-chloroethyl)phosphonic acid

CAS (*P*)-(2-chloroethyl)phosphonic acid

Structural formula



Molecular formula

$C_2H_6ClO_3P$

Relative molecular mass

144.5

CAS Registry number

16672-87-0

CIPAC number

373

Identity tests

Retention time in ion chromatography, ^{1}H-NMR

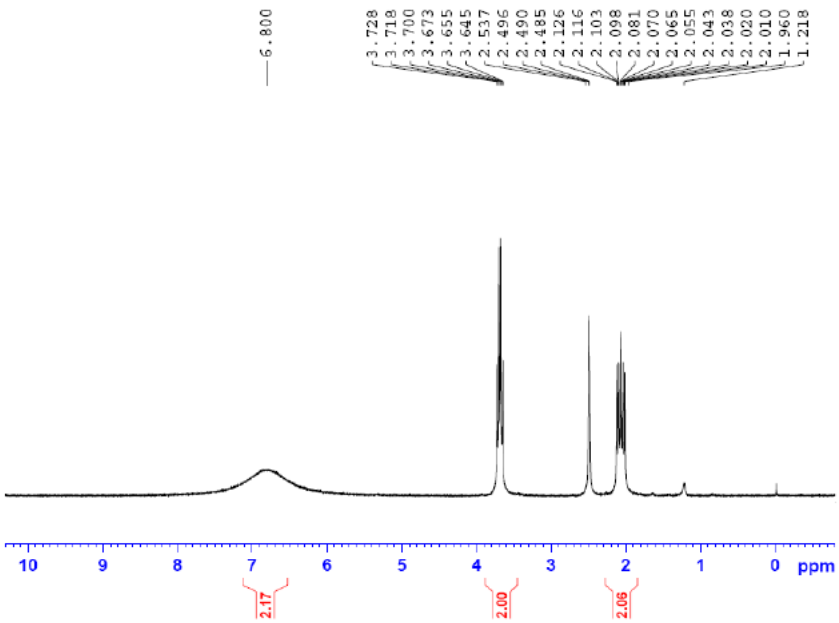


Table 1. Physico-chemical properties of pure ethephon

Parameter	Value(s) and conditions	Purity %	Method reference (and technique if the reference gives more than one)	Study number
Vapour pressure	<1.0 x 10^{-3} Pa (from 18 to 80 °C)	98.5	OECD 104, by extrapolation	EFSA Scientific Report (2008) 174
Melting point	72.0-73.6 °C	93.0	OECD 102	BGP-2019-008
Temperature of decomposition	-	-	-	-
Solubility in water	>1000 g/l at 20 °C pH < 2	93.0	OCED 105	BGP-2019-008
Octanol/water partition coefficient	log P_{OW} = -0.53 at 20 °C	93.0	OCED 107	BGP-2019-008
Hydrolysis characteristics	Half-life =73.5 days at pH 5, 2.4 days at pH 7 and 1.0 day at pH 9 (all 25 °C)	97.5% radio chem. pure	Not stated	EFSA Scientific Report (2008) 174

Photolysis characteristics	Ethephon (at 25 °C and pH 5): rate constant k2 under irradiated conditions $9.39X10^{-04}$ h^{-1} (DT_{50} 61 days of 12 hr irradiation/day). rate constant k1 under non-irradiated conditions $5.22X10^{-04}$ h^{-1} (DT_{50} 111 days of 12 hr darkness/day). Net rate constant k3 (DT_{50}) due to irradiation alone: k3 = k2 – k1 = $4.17E^{-04}$ h^{-1} (Net half-life 139 days of 12 hr irradiation/day). (Linear-regression) Only degradation product is ethylene, max. 15.3% and 23.1% in non-irradiated and irradiated samples.	Not stated	Not stated	EFSA Scientific Report (2008) 174
Dissociation characteristics	pKa1= 2.29 pKa2= 7.19	93.0	OECD 112, titration method	BGP-2019-008
Solubility in organic solvents	methanol >1000 g/L *n*-octanol 537740 mg/L *n*-hexane < 19.47 mg/L toluene < 19.47 mg/L dichloromethane 1006.3 mg/L ethyl acetate 280090 mg/L	93.0	OCED 105	BGP-2019-008

Table 2. Chemical composition and properties of ethephon 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. Mass balances were 98.04 – 98.22 % and percentages of unknowns were 1.79 – 1.94%.		
Declared minimum ethephon content		930 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		
Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC and/or TK	72.0-73.6 °C	93.0	OECD 102	BGP-2019-008

Formulations

The main formulation type available is SL.

This formulation is registered and sold in many countries in North, Central and South America, Europe, Asia, Africa and Oceania.

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests) is ion chromatography. The ethephon is separated by an anion exchange column, and determined using a conductivity detector and external standardisation.

The method(s) for determination of impurities are based on ion chromatography and gas chromatography.

The relevant impurity MEPHA is separated by an anion exchange column, and determined using a conductivity detector and external standardisation. 1,2-dichloroethane is separated by a ZB-Wax capillary column, and determined using a flame ionisation detector and internal standardisation.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD 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 SL formulations, comply with the requirements of the FAO/WHO Manual (2022 edition).

Containers and packaging

Ethephon and its formulations have corrosive properties and the containers for ethephon TC, TK and SL have to be high-density polyethylene (HDPE).

Expression of the active ingredient

The ethephon content is expressed as ethephon.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Notes.

(i) The proposer confirmed that the toxicological and ecotoxicological data included in the summary below were derived from ethephon having impurity profiles similar to those referred to in the table above.

(ii) The conclusions expressed in the summary below are those of the proposer, unless otherwise specified.

Table 3. Toxicology profile of the ethephon technical material, based on acute toxicity, irritation and sensitization

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Rat, female	oral	93.51	OECD TG 425, 14 days, 1330, 1710 and 2000 mg/kg bw	LD_{50} = 2000 mg/kg bw	20-213-001
Rat, female	dermal	93.51	OECD TG 402, 14 days, 2000 mg/kg bw	$LD_{50} \geq$ 2000 mg/kg bw	20-213-002
Rat, male and female	inhalation	93.51	OECD TG 403, 14 days, 5.04 mg/L (max. attainable concentration)	LC_{50} > 5.04 mg/L	20-213-003
-	skin irritation	-	OECD GD 263	Serious skin damage (pH < 2)	-
-	eye irritation	-	OECD GD 263	Serious eye damage (pH < 2)	-
Guinea pig, male	skin sensitisation	93.51	OECD TG 406, 14 days, 5.0% (w/v) in distilled water	Not a skin sensitiser	20-213-004

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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Rats, males and females	Oral (gavage)	93.1%	OECD 407, 28 days. 0, 30, 150 and 750 mg/kg bw/day	NOAEL = 30 mg/kg bw/day for males and females	S210710010
Mice, males and females	Oral (dietary)	71.3%	OECD 407, 28 days. 0, 5.3, 18, 51, 181 and 546 mg/kg bw per day for males and 0, 6.5, 22, 69, 210 and 635 mg/kg bw per day for females, respectively	NOAEL = 22 mg/kg bw/day for males and females	M-187702-01-1 (JMPR report 2015)
Dogs, males and females	Oral (dietary) long term toxicity	Not stated	Guideline not stated, 2 years. 0, 0.86, 7.6 and 42.2 mg/kg bw per day for males and 0, 0.86, 8.4 and 47.8 mg/kg bw per day for females, respectively	NOAEL = 0.86 mg/kg bw/ day	JMPR report 2015
Mice	Carcinogenicity (dietary)	Not stated	Guideline not stated, 78 weeks. 0, 4.5, 45 and 150 mg/kg bw per day, respectively	NOAEL = 4.5 mg/kg bw per day, based on reduction of erythrocyte AChE activity observed at weeks 52 and 78 in females at 45 mg/kg bw per day. No treatment-related tumours were observed in mice in this study.	JMPR report 2015
Rats, males and females	Two-generation reproductive toxicity (dietary)	Not stated	0, 22, 220 and 2260 mg/kg bw per day for F_0 males and 0, 25, 260 and 2570 mg/kg bw per day for F_0 females, respectively; and 0, 20, 200 and 2220 mg/kg bw per day for F_{1b} males and 0, 24, 245 and 2520 mg/kg bw per day for F_{1b} females, respectively	NOAEL for parental toxicity was 20 mg/kg bw per day, based on an increased incidence of loose faeces in F_{1b} males at 3000 ppm (equal to 200 mg/kg bw per day). The NOAEL for offspring toxicity was 22 mg/kg bw per day), based on an increased mortality in F_{1b} pups from PND 4 to PND 7 and a reduction in body weight gain during lactation in F_{2b} pups at 3000 ppm (equal to 220 mg/kg bw per day).	JMPR report 2015

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
				The NOAEL for reproductive toxicity was 2220 mg/kg bw per day, the highest dose tested.	
Rats	Developmental toxicity (gavage)	Not stated	0, 200, 600 or 1800 mg/kg bw per day	NOAEL for maternal toxicity was 600 mg/kg bw per day, based on increased mortality, clinical signs (salivation), reduced body weight gain, and various macroscopic findings and histological changes (focal lymphoid hyperplasia of the spleen and focal parenchymal fibrosis of the liver) at 1800 mg/kg bw per day. The NOAEL for embryo and fetal toxicity was 1800 mg/kg bw per day, the highest d se tested.	JMPR report 2015
Rats	Neurotoxicity (gavage)	Not stated	13 weeks. 0, 75, 150 or 400 mg/kg bw per day (the high dose was decreased to 300 mg/kg bw per day during week 10/11 of treatment)	The NOAEL was 75 mg/kg bw per day, based on reduction of erythrocyte cholinesterase in females at 150 mg/kg bw per day	JMPR report 2015

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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Salmonella typhimurium strains TA1537, TA1535, TA98, TA100 and TA102	Bacterial Reverse Mutation Test, *in vitro*	93.0	OECD TG 471, 0.312, 0.625, 1.25, 2.5 and 5.0 mg/plate, in the absence and presence (5 %v/v) of metabolic activation system	Non mutagenic	19001
Chinese Hamster Ovary cells, HGPRT-locus	Gene mutation	-	0.5, 1.0, 2.0, 2.5, 3.0,3.5, 4.0, 5.0 mg/ml without S-9 mix 0.5, 1.0, 2.0, 2.2, 2.4,2.6, 2.8, 3.0 mg/ml with S-9 mix	Negative	EFSA 2017
Chinese Hamster Ovary cells	Chromosomal aberration	-	753, 1000, 1510, 2010µg/ml without S-9 mix502, 1000, 1510, 2010 µg/ml with S-9 mix.	Negative	EFSA 2017
Rat primary hepatocytes	Unscheduled DNA synthesis (UDS) *in vitro*	-	25, 50, 100, 250, 100,500, 1000, 2000 µg/ml	Negative	EFSA 2017

Table 6. Ecotoxicology profile of the technical material

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Daphnia magna	Acute toxicity	74.0	OECD TG 202, 0, 1, 10 and 100 mg/l. 48 hr.	EC_{50} > 100 mg/l	EFSA 2017
Rainbow trout	Acute toxicity	72.1	OECD TG 203, 251, 100, 180, 320, 560 and 1000 mg/l. 96 hr.	LC_{50} = 519 mg/l	EFSA Scientific Report (2008) 174
Chlorella vulgaris	Algae growth inhibition	72.1	OECD TG 201, 0, 5, 10, 20, 40 and 80 mg/L. 72hr	EC_{50} = 33 mg/l NOEC = 5 mg/l	EFSA 2017
Earthworm	Sub-lethal effects	71.4	ISO 11268-2 and BBA VI 2-2. 0, 12.5, 25, 50, 100 and 200 mg/kg.	NOEC > 200 mg/kg dry soil	EFSA 2017
Apis mellifera (honey bee)	Acute oral toxicity	71.9	EPPO Guideline 170. Contact: 6.3, 12.5, 25, 50 and 100 µg/bee, 48 hr Oral: 7.3, 14.2, 28.5, 58.5 and 116.5 µg/bee, 48 hr	Contact: LD_{50} > 100 µg/bee Oral: LD_{50} >1 16.5 µg/bee	EFSA 2017
Bobwhite quail	acute toxicity	71.3	OECD TG 205, 251, 398, 631, 1000 and 1500 mg/kg bw. 14 days.	LD_{50} = 764 mg/kg bw	EFSA Scientific Report (2008) 174
Japanese quail	Reproduction toxicity	71.6	OECD TG 206, 251, 160, 400 and 1000 mg/kg diet. 6 weeks.	NOEC = 1000 mg/kg diet	EFSA 2017

Ethephon has not been evaluated by the WHO IPCS, but was evaluated by the FAO/WHO JMPR for residues in 1994 and 2015, and for toxicity in 1995, 1997, 2002 and 2015.

The classification of Ethephon by ECHA under CLP is :

Acute toxicity - Category 4, Oral

Acute toxicity - Category 3, Dermal

Skin corrosion, Sub-category 1C

Acute toxicity - Category 4, Inhalation

Hazardous to the aquatic environment, long-term (Chronic) - Category Chronic 2.

GHS Hazard statement(s) :

H302 Harmful if swallowed

H311 Toxic in contact with skin

H314 Causes severe skin burns and eye damage

H332 Harmful if inhaled

H411 Toxic to aquatic life with long lasting effects

ANNEX 2

REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
JMPR, 2015 a	FAO/WHO	2015	Pesticide residues in food 2015. Joint FAO/WHO Meeting on Pesticide Residues. FAO PLANT PRODUCTION AND PROTECTION PAPER 223. Non-GLP. FAO. Published. https://www.fao.org/3/i5186e/i5186e.pdf, p.131
JMPR, 2015 b	FAO/WHO	2015	Pesticide residues in food 2015. Joint FAO/WHO Meeting on Pesticide Residues. FAO PLANT PRODUCTION AND PROTECTION PAPER 223. Non-GLP. FAO. Published. https://www.fao.org/fileadmin/user_upload/IPM_Pesticide/JMPR/Evaluations/2015/ETHEPHON__106_.pdf, p.581
AGP:CP/367	FAO	2000	https://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Specs/ETHEPHON.pdf
FAO/WHO Manual	FAO/WHO	2022	Manual on the development and use of FAO and WHO specifications for chemical pesticides, second edition. https://www.fao.org/3/cb8401en/cb8401en.pdf
-	Chen	2022	E-mail from Tienchun Chen, sent on 19 September 2022 [From: chentienchun@caas.cn to bura.laszlo.id@gmail.com]
CIPAC, F	Martijn A. and Dobrat W.	1995	CIPAC Handbook Volume F. Physico-chemical Methods for Technical and Formulated Pesticides
CIPAC, J	Martijn A. and Dobrat W.	2000	CIPAC Handbook Volume J. Analysis of Technical and Formulated Pesticides
CIPAC, O	Cardeal de Oliveira M.C. and Garvey J.	2017	CIPAC Handbook Volume O. Analysis of Technical and Formulated Pesticides
CIPAC, P	Garvey J. and Patrian B.	2021	CIPAC Handbook Volume P. Analysis of Technical and Formulated Pesticides
EFSA Scientific Report (2008) 174	EFSA	2008	Conclusion regarding the peer review of the pesticide risk assessment of the active substance ethephon. Non-GLP, EFSA, published: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2006.174r
EFSA 2017	EFSA	2017	Dossier for the evaluation of the active substance Ethephon (CAS No. 16672-87-0) according to Regulation (EC) No. 1107/2009, Document MCA, S8. Non-GLP, EFSA, Published: https://open.efsa.europa.eu/affdbd7f-cd4d-4afa-9461-dd4a42738a6b.
BGP-2019-008	B. Yang	2019	Chemical and Physical Characterization of Ethephon TC: Color, Physical State, Odor, Density, Partition Coefficient, Dissolution Constant, Stability, Melting Point and Solubility. Study BGP-2019-008. GLP. BioGuide Technologies Co., Ltd., China. Unpublished.
20-213-001		2020	Acute Oral Toxicity Study of Ethephon Technical (Up and Down Procedure) in Wistar Rats. Study 20-213-001. GLP. GLP. Unpublished.
20-213-002		2020	Acute Dermal Toxicity Study of Ethephon Technical in Wistar rats. Study 20-213-002. GLP. GLP. Unpublished.
20-213-003		2020	Acute Inhalation Toxicity Study of Ethephon Technical in Wistar Rats. Study 20-213-003. GLP. GLP. Unpublished.

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
20-213-004		2020	Skin Sensitization Maximization Study of Ethephon Technical in Guinea pigs. Study 20-213-004. GLP. GLP. Unpublished.
S210710010		2022	Repeated Dose 28-Day Oral Toxicity Study of Ethephon technical in Rats. Study S210710010. GLP. GLP. Unpublished.
19001	C. Sekhar	2019	Bacterial Reverse Mutation Test with Ethephon 91% Tech using *Salmonella typhimurium*. Study S210710010. GLP. PALAMUR BIOSCIENCES PRIVATE LIMITED (PBS), India. GLP. Unpublished.