FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

CHLORMEQUAT CHLORIDE

2-chloroethyltrimethylammonium chloride

FOOD AND AGRICULTURE ORGANIZATION of THE UNITED NATIONS

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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.

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

INTRODUCTION

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

Since 1999, the development of FAO specifications has followed the **New Procedure**, first described in the 5th edition of the "Manual on the development and use of FAO specifications for plant protection products" (FAO Plant Production and Protection Paper No. 149) and, subsequently, in the 1st edition of the "Manual for Development and Use of FAO and WHO Specifications for Pesticides" (FAO Plant Production and Protection Paper No. 173, 2002). 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).

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** was changed. Every specification now consists 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 9 of the 1st edition of the "FAO/WHO Manual on Pesticide Specifications."

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 those 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.

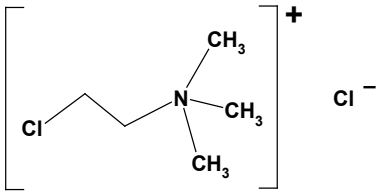
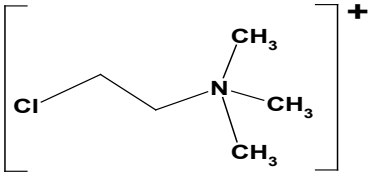
* Footnote: The publications are available on Internet under (http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/en/).

PART ONE

SPECIFICATIONS

CHLORMEQUAT CHLORIDE

INFORMATION

	Salt	Cation
ISO common name:	chlormequat chloride	chlormequat (BSI; E-ISO, (*m)*F-ISO) (Note 1)
Synonyms :	CCC, Chlorocholine chloride	
Chemical names		
IUPAC:	2-chloroethyltrimethyl ammonium chloride	2-chloroethyltrimethyl ammonium
CA:	2-chloro-*N,N,N*-trimethylethanaminium chloride	2-chloro-*N,N,N*-trimethylethanaminium
Structural formula:		
Molecular formula:	$C_5H_{13}Cl_2N$	$C_5H_{13}ClN$
Relative molecular mass:	158.1	122.6
CAS Registry number:	999-81-5	7003-89-6
CIPAC number:	143.302	143
Identity tests:	Cation: retention time in non-suppressed ion-chromatography on silica-based cation exchange column (CIPAC Handbook H, p. 77, 1998) or IR spectrum. Anion: precipitation of AgCl on addition of $AgNO_3$ solution.	Retention time in non-suppressed ion-chromatography on silica-based cation exchange column (CIPAC Handbook H, p. 77, 1998) or IR spectrum.

Note 1. The ISO common name, chlormequat, applies to the cation, with the requirement that the salt is identified. In this case, the salt is chlormequat chloride.

CHLORMEQUAT CHLORIDE TECHNICAL CONCENTRATE

FAO specification 143.302/TK (August 2005*)

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 (143.302/2003). 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 (143.302/2003), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of chlormequat chloride together with related manufacturing impurities and shall be a pale yellow to yellow liquid with a moderately fish-like odour, free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (143/TK/M2/2 CIPAC Handbook H, p. 77, 1998)

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 **Chlormequat chloride content** (143/TK/M2/3 CIPAC Handbook H, p. 77, 1998)

The chlormequat chloride content shall be declared (not less than 750 g/l at 20 ± 2°C, corresponding to 658 g/kg, Note 1) and, when determined, the average measured content shall not differ from that declared by more than ± 25 g/kg or g/l.

3 Relevant impurities

3.1 1,2-dichloroethane (Note 2)

Maximum: 0.1 g/kg of the dry chlormequat chloride content found under 2.2, above.

Note 1 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 2 The analytical method for determination of 1,2-dichloroethane is available from the Pesticide Management Group of the FAO Plant Protection Service or can be downloaded here.

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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/agriculture/crops/core-themes/theme/pests/jmps/en/

CHLORMEQUAT CHLORIDE SOLUBLE CONCENTRATE

FAO specification 143.302/SL (August 2005*)

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 (143.302/2003). 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 (143.302/2003), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of technical chlormequat chloride, complying with the requirements of FAO specification 143.302/TK (August 2005), dissolved in suitable solvents, together with any other necessary formulants. It shall be in the form of a clear or opalescent 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 (143/SL/M2/2 CIPAC Handbook H, p. 80, 1998)

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 Chlormequat chloride content (143/TC/M2/3 CIPAC Handbook H, p. 80, 1998)

The chlormequat chloride content shall be declared (g/kg or g/l at 20 ± 2°C, Note 1) and, when determined, the average measured content shall not differ from that declared by more than the following tolerance:

Declared content in g/kg or g/l at 20 ± 2°C	Tolerance
above 25 up to 100	± 10% of the declared content
above 100 up to 250	± 6% of the declared content
above 250 up to 500	± 5% of the declared content
above 500	± 25 g/kg or g/l
Note in each range the upper limit is included	

3 Relevant impurities

3.1 1,2-dichloroethane (Note 2)

Maximum: 0.1 g/kg of the dry chlormequat chloride content found under 2.2, above.

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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/agriculture/crops/core-themes/theme/pests/jmps/en/

4 Physical properties

4.1 **pH range** (MT 75.2, CIPAC Handbook F, p. 206, 1995) (Note 3)

pH range: 2.5 to 8.

4.2 **Solution stability** (MT 41, CIPAC Handbook F, p. 131, 1995)

The formulation, after the stability test at 54 °C and following dilution (Note 4) with CIPAC standard D and standing at 30 ± 2°C for 18 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 45 µm test sieve.

4.3 **Persistent foam** (MT 47.2, CIPAC Handbook F, p. 152, 1995) (Note 5)

Maximum: 30 ml after 1 minute.

5 Storage stability

5.1 **Stability at 0°C** (MT 39.2, CIPAC Handbook F, p. 128, 1995)

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 46.3, CIPAC Handbook J, p.128, 2000)

After storage at 54 ± 2 °C for 14 days, the determined average active ingredient content must not be lower than 95 % relative to the determined average content found before storage (Note 6) and the product shall continue to comply with the clauses for pH range (4.1), as required.

Note 1 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 2 The analytical method for determination of 1,2-dichloroethane is available from the Pesticide Management Group of the FAO Plant Protection Service or can be downloaded here.

Note 3 The pH shall be measured in a solution of 2 g sample in 100 ml CIPAC water D.

Note 4 The concentration used for the test should not be higher than the highest concentration recommended in the instruction for use.

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

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

PART TWO

EVALUATION REPORTS

CHLORMEQUAT CHLORIDE

CHLORMEQUAT CHLORIDE

EVALUATION REPORT 143.302/2003

Explanation

The data for chlormequat chloride were evaluated in support of new FAO specifications for TK and SL.

Chlormequat chloride is not under patent.

Chlormequat was evaluated by the FAO/WHO JMPR in 1970, 1972, 1994 and 1997. It will be reviewed by the European Commission according to Commission regulation (EC) No. 451/2000 in 2004. Chlormequat chloride is registered in many countries of Europe, North- and South-America, Asia, and in Australia.

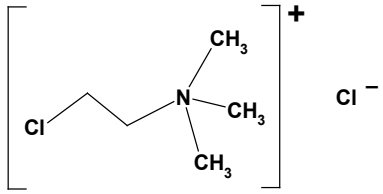
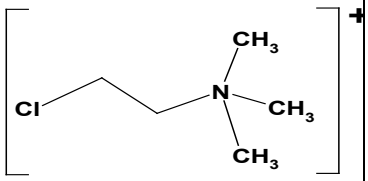
The draft specification and the supporting data were provided by BASF Aktiengesellschaft, Nufarm GmbH & Co KG, Ciba Speciality Chemicals and Taminco n.v., in 2002.

Uses

Chlormequat is a plant growth regulator which inhibits cell elongation, hence shortening and strengthening stems and producing sturdier plants. It also influences the developmental cycle, leading to increased flowering, for example. It may also increase chlorophyll formation and root development. Chlormequat chloride is used to increase resistance to lodging (by shortening and strengthening stems) and to increase yields in wheat, rye, oats, and triticale. It is also used to promote lateral branching and flowering in azaleas, fuchsias, begonias, poinsettias, pelargoniums, and other ornamental plants. It is also used on cotton. (Pesticide Manual 1997)

Identity of the active ingredient

	Salt	Cation
ISO common name:	chlormequat chloride	chlormequat (BSI; E-ISO, (*m)*F-ISO) (Note 1)
Synonyms:	CCC, chlorocholine chloride	
Chemical names:		
IUPAC:	2-chloroethyltrimethyl ammonium chloride	2-chloroethyltrimethyl ammonium
CA:	2-chloro-*N,N,N*-trimethylethanaminium chloride	2-chloro-*N,N,N*-trimethylethanaminium

	Salt	Cation
Structural formula:		
Molecular formula:	$C_5H_{13}Cl_2N$	$C_5H_{13}ClN$
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Note 1. The ISO common name, chlormequat, applies to the cation, with the requirement that the salt is identified. In this case, the salt is chlormequat chloride.

Physical and chemical properties of chlormequat chloride

Table 1 Physico-chemical properties of pure chlormequat chloride.

Parameter	Value(s) and conditions	Purity %	Method reference	Company, year
Vapour pressure	<1 x 10^{-6} Pa at 20°C (extrapolated)	99.9	OECD 104, by extrapolation	BASF, 2001
Melting point and temperature of decomposition	Melting point: 236°C, with decomposition	99.5	OECD 102	BASF, 2001
Solubility in water	>500 g/l at 20°C at pH 4 (buffer). >500 g/l at 20°C at pH 7 (buffer). >500 g/l at 20°C at pH 9 (buffer). >500 g/l at 20°C in de-ionized water	99.5	EEC A6, OECD 105 (flask method)	BASF, 2000
Octanol/water partition coefficient	log P_{OW} = -3 at 20°C in de-ionized water and at pH 4, 7 and 9.	99.5	EEC A8	BASF, 2000
Hydrolysis characteristics	Half-life = >1 year at 25°C at pH 4, 7 and 9. Test conditions: 50°C for 5 days, <5 % degradation	>99	OECD 111	Agrolinz/Melamin Task Force, 1995

Parameter	Value(s) and conditions	Purity %	Method reference	Company, year
Photolysis characteristics	Half-life = 201 d at 20°C and pH 5.4. Half life calculated from quantum yield of direct photo-transformation. Quantum yield ϕ (PHI): 4.74 x 10^{-7}.	Radiochemical purity ≥ 98.0, 555 MBq/mmol	OECD Draft Test Guideline (1990): Photo-transformation of chemicals in water	RCC Task Force, 1993
Dissociation characteristics	pKa is not applicable (a free base does not exist) but the salt is fully dissociated.	-	-	-

Table 2. Chemical composition and properties of chlormequat chloride technical material (TK).

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO. Mass balances were 99.0-102.1% and percentages of unknowns were <0.1% (Note 1).
Declared nominal chlormequat chloride content	750 g/l, corresponding to 658 g/kg and a minimum of 960 g/kg in water-free technical chlormequat chloride (Note 1). Tolerances of ± 25 g/l or g/kg apply to the nominal content of the TK.
Relevant impurities ≥1 g/kg and maximum limits for them	None
Relevant impurities <1 g/kg and maximum limits for them:	1,2-dichloroethane: 0.1 g/kg of chlormequat chloride content (Note 1).
Stabilizers or other additives and maximum limits for them:	None.
Melting or boiling temperature range of the TC (dried TK) (Note 1)	235-236°C, with decomposition.

Note 1. Chlormequat chloride is very hygroscopic and, in practice, chlormequat chloride is produced and handled as an aqueous solution TK, with a nominal chlormequat chloride content of 750 or 780 g/l. Five-batch analyses were conducted using technical concentrate samples but the results were calculated on the basis of dry chlormequat chloride. On a water-free basis, the minimum purity of the technical chlormequat chloride is 960 g/kg. Concentrations of the relevant impurity are expressed as g/kg of dry chlormequat chloride.

Toxicological summaries

Notes.

(i) The proposer confirmed that the toxicological and ecotoxicological data included in the summary below were derived from chlormequat chloride 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 chlormequat chloride technical material, based on acute toxicity, irritation and sensitization.

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Company, year
Rat (m, f)	Oral	66.1	EPA Subdiv. F, § 81-1	LD_{50} = 522 mg/kg bw	BASF, 1990
Mouse	Oral	98	OECD (401) (1982)	LD_{50} = 589 mg/kg bw	BASF, 1975

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Company, year
(m,f)					
Rat (m, f)	Dermal	n.r.	24 h exposure to the intact skin, OECD (402)	LD_{50} = >4000 mg/kg bw	BASF, 1978
Rabbit (m, f)	Dermal	66.1	EPA Subdiv. F, § 81-2, 24h	LD_{50} = 1250 mg/kg bw	BASF, 1990
Rat (m, f)	Inhalation	99.0	EPA Subdiv. F, § 81-3, 4h	LC_{50} = >4570 mg/m^3	BASF, 1990
Rabbit (m)	Skin irritation	66.1	EPA Subdiv. F, § 81-5	Non-irritant	BASF, 1990
Rabbit (m, f)	Eye irritation	66.1	EPA Subdiv. F, § 81-4	Non-irritant	BASF, 1990
Guinea pig (m)	Skin sensitization	nr	Based on Buehler, E.V.: Delayed Contact Hypersensitivity in the Guinea Pig, Arch. Dermat. 92, 171-175 (1965) EPA Subdiv. F, § 81-6	Non-sensitizing	BASF, 1990
Guinea pig (m)	Skin sensitization	67.4	Based on Magnusson, B. and Kligmann, A.M.: The Guinea Pig Maximization Test, J. Invest. Dermatol. 52, 268-276 (1969))	Non-sensitizing	BASF, 1992

nr = not reported.

Chlormequat chloride is of moderate acute oral and low inhalation toxicity. It is not irritant to the skin or eye in rabbits. It does not cause delayed contact hypersensitivity in guinea pigs, by Buehler or Magnusson and Kligmann tests.

Table 4. Toxicology profile of chlormequat chloride technical material based on repeated administration (sub-acute to chronic).

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Company, year
Rabbit (m, f)	Dermal	99	21 d, EPA Subdiv. F , § 82-2	NOEL = 150 mg/kg bw/d	BASF, 1981
Mouse (m, f)	Oral, sub-acute	66.7	28 d, OECD (407)	NOAEL > 885 mg/kg bw/d (males) NOAEL > 1190 mg/kg bw/d (females)	BASF, 1990
Rat (m, f)	Oral, sub-acute	66.7	28 d, OECD (407)	NOAEL = 137 mg/kg bw/d (males) NOAEL = 148 mg/kg bw/d (females) LOEL = 275 mg/kg bw/d	BASF, 1990
Dog (m, f)	Oral, sub-acute	67.4	28 d, OECD (407) without histopathology	NOAEL = 9 mg/kg bw/d LOEL = 13 mg/kg bw/d	BASF, 1993

Species	Test	Purity %	Duration and conditions or guideline adopted	Result	Company, year
Mouse (m, f)	Oral, sub-chronic	67.4	3 mo, OECD (408), EPA Subdiv. F, §82-1	NOAEL > 1070 mg/kg bw/d (males) NOAEL > 1400 mg/kg bw/d (females)	BASF, 1991
Rat (m, f)	Oral, sub-chronic	97	3 mo, OECD (408)	NOAEL = 61 mg/kg bw/d (males) NOAEL = 220 mg/kg bw/d (females) LOEL = 220 mg/kg bw/d	BASF, 1981
Dog (m, f)	Oral	67.4	12 mo, OECD (452), EPA Subdiv. F, § 83-1, Japan MAFF (1985)	NOAEL = 4.7 mg/kg bw/d LOEL = 32 mg/kg bw/d	BASF, 1993
Rat (m, f)	Feeding, chronic toxicity	67.4	18 mo, OECD(452), EPA Subdiv.F, § 83-1	NOAEL = 50 mg/kg bw/d (males and females) LOEL = 154 mg/kg bw/d	BASF, 1992
Mouse (m, f)	Feeding, carcinogenicity	67.4	110 weeks, OECD (451), EPA Subdiv. F, § 82-2	NOAEL = 84 mg/kg bw/d (males) NOAEL = 390 mg/kg bw/d (females) Not carcinogenic	BASF, 1994
Rat (m, f)	Feeding, carcinogenicity	67.4	24 mo, OECD(451), EPA Subdiv.F, § 83-2	NOAEL = 49 mg/kg bw/d Not carcinogenic	BASF, 1992
Rat (m, f)]	Feeding, 2 generation reproduction	67.4	OECD (416), EPA Subdiv. F, § 83-4, Japan MAFF (1985)	No adverse effects on fertility NOAEL = 91 mg/kg bw/d (reproduction) NOAEL = 91 mg/kg bw/d (systemic toxicity for F0 males, F1a, F1b, F2 male and female) NOAEL = 30 mg/kg bw/d (systemic toxicity for F0 females)	BASF, 1993
Rabbit (m, f)	Teratogenicity and developmental toxicity	75.7	OECD (414), EPA Subdiv. F, § 83-3 (1982)	Not teratogenic, not foetotoxic, NOAEL = 20 mg/kg bw/d (foetotoxicity) NOAEL = 10 mg/kg bw/d (maternal toxicity)	RCC, 1992 BASF, 1978
Rat (m, f)	Embryotoxicity/ teratogenicity	75.7	OECD (414), EPA Subdiv. F, § 83-3 (1982)	Not teratogenic, not foetotoxic, no reproductive effects NOAEL = 225 mg/kg bw/d (embryo/foetotoxicity) NOAEL = 25 mg/kg bw/d (maternal toxicity)	Agrolinz RCC, 1992

Chlormequat chloride is of moderate toxicity from both oral and dermal administration. Long-term studies indicated no special target organ. Repeated oral administration resulted in diarrhoea, vomiting and salivation (dog), reduced body

weight (rat), or down-growth in the ovaries (mouse) and endometrial hyperplasia (mouse).

Chlormequat chloride was not carcinogenic in long-term studies in rats and mice, after administration via the diet. Chlormequat chloride did not lead to malformations in rats and rabbit. There were no indications of any impairment of fertility in animal studies.

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

Species	Test	Purity %	Conditions	Result	Company, year
Salmonella. typhimurium	Point mutation, Ames test	66.1	Dose range: up to 5000µg/plate with (S-9 from S.D. rats) and without metabolic activation in TA 98, TA 100, TA 1535, TA 1537, TA 1538 strain	Not mutagenic	BASF, 1990, ACC
Escherichia coli	Point mutation, Ames test	66.1	Dose range: up to 5000µg/plate with (S-9 from S.D. rats) and without metabolic activation in WP-2 uvrA	Not mutagenic	BASF, 1990, ACC
Chinese hamster ovary (CHO) cell line	Point mutation, CHO/HGPRT test	66.1	Dose range: up to 5000 µg/ml with (S-9 from S.D. rats) and without metabolic activation	Not mutagenic	BASF, 1990, ACC
Human lymphocytes	Chromosome aberration, cytogenic investigation, *in vitro*	94.5 to 98.9	Dose range: up to 5000 µg/ml with and without metabolic activation (S9-mix from Sprague Dawley rats)	Not mutagenic	BASF, 1987, Notox
Bone marrow cells (mice)	Chromosome aberration, micronucleus test, *in vivo*	94.5 to 98.5	Two-fold oral administration, dose range: 8.1-202.5 mg/kg bw	Not mutagenic	BASF, 1983, RCC
Bone marrow cells (Sprague Dawley rats)	Chromosome aberration, cytogenic investigation, *in vivo*	66.1	Oral administration, dose range: 0, 125-500 mg/kg bw	Not mutagenic	BASF, 1991, ACC
Rat hepatocytes (Sprague Dawley rats)	DNA damage and repair, unscheduled DNA synthesis, *in vitro*	66.1	Dose range 0.63-7.5 µg/ml	Not mutagenic	BASF, 1990, SITEK

The genotoxic potential of chlormequat chloride was tested against the endpoints of gene mutation, chromosome damage as well as DNA damage and repair. The *in vitro* system of human lymphocytes, as well as the *in vivo* studies performed with mice and rats, gave no indication of chromosome aberration. No DNA damage and repair were observed in the studies. Chlormequat chloride was thus found to be devoid of mutagenic activity on the basis of the studies performed.

Table 6. Ecotoxicology profile of chlormequat chloride technical material.

Species	Test	Purity %	Duration and conditions	Result	Company, year
Daphnia magna (water flea)]	Acute toxicity	100	48 h, static water, OECD (202)	EC_{50} = 31.7 mg/l	UCB
Daphnia magna (water flea)]	Chronic toxicity	95.6	21 d, flow through, EPA Subdiv. E § 72-4	NOEC = 5 mg/l	BASF
Salmo gairdneri (rainbow trout)	Acute toxicity	100	96 h, static water, EPA Subdiv. E § 72-1	LC_{50} = 2147 mg/l	UCB
Oncorhynchus mykiss (rainbow trout)	Sub-lethal toxicity	95.6	28 d , flow through, OECD (204)	NOEC >100 mg/l	BASF, 1991
Cyprinus carpio L.(common carp)	Acute toxicity	95.6	96 h, static, OECD (203)	NOEC >100 mg/l	BASF, 1991
Pseudokirchneriella subcapitata (green alga)	Acute toxicity	66.1	96 h, static water, OECD (201)	EC_{10} >100 mg/l (growth rate) EC_{10} >100 mg/l (biomass) no morphological effects observed.	BASF, 2001
Lemna gibba (Duckweed)	Acute toxicity	66.1	7 d, OECD Draft Guideline (1998), EPA 712-C-96-156, OPPTS 850.4400 (1996)	EC_{50} = 28 mg/l NOEC = 0.1 mg/l	Task Force, 2001
Pseudomonas putida	Growth inhibition test	66.7	DIN 38412 (part 8), DIN 38404 (part 2)	NOEC >1522 mg/l	BASF, 1988
Eisenia foetida (Earthworm)	Acute toxicity	100	14 d, OECD (207)	LC_{50}= 2931.5 mg/kg dry soil NOEC = 300 mg/kg dry soil	UCB
Apis mellifera (honey bee)	Acute oral toxicity	99.5	48 h, OECD (213), and according to recommendations of ICPBR (1999)	LD_{50} >109.5 µg/bee	BASF, 2000
Apis mellifera (honey bee)	Contact toxicity	99.5	48 h, OECD (214), and according to recommendations of ICPBR (1999)	LD_{50} >100 µg/bee	BASF, 2000
Japanese quail	Acute toxicity	100	21 d	LD_{50} = 440 mg/kg bw	Nufarm
Japanese quail	Dietary toxicity	100	8 d, OECD (205)	LC_{50} >313.3 mg/kg bw	UCB, 1993
Japanese quail	Reproduction toxicity	66.9	6 weeks treatment, OECD draft guidelines (1999)	LC_{50}= 1000 mg/kg diet NOEC = 400 mg/kg diet	Task Force, 2001
Mallard duck	Short-term toxicity	66.9	5 d, OECD (205), EPA Subdiv. E § 71-2	LC_{50} >5620 mg/kg diet NOEC = 3160 mg/kg diet	Task Force, 2001

The ecotoxicological effects of chlormequat chloride were investigated using various organisms from major ecotoxicological groups. The results demonstrated that chlormequat chloride is of low toxicity to a broad range of aquatic and terrestrial organisms including fish, algae, birds and terrestrial invertebrates. Chlormequat chloride is of moderate toxicity only towards aquatic invertebrates (Daphnia).

Chlormequat was evaluated by the FAO/WHO JMPR in 1970, 1972, 1994 and 1997. The conclusions (JMPR 1997) indicated that chlormequat was of moderate acute oral and dermal toxicity (LD_{50} = 200-1000 mg/kg bw), with rabbits and dogs being the most sensitive species (LD_{50} = 50-80 mg/kg bw). It was not carcinogenic and not teratogenic. The JMPR also concluded that chlormequat was not genotoxic, *in vivo* or *in vitro*, it was not irritating to the eye or skin of rabbits and did not cause delayed hypersensitivity. An ADI of 0-0.05 mg/kg bw was allocated, based on the one-year study of toxicity in dogs as most sensitive species.

The WHO hazard classification of chlormequat chloride is: Class III, slightly hazardous (WHO 2002).

Formulations and co-formulated active ingredients

The main formulation type is soluble concentrate (SL). Examples of trade names of the solo formulations are Chlormequatchlorid, CeCeCe, Cycocel, Stabilan and Belcocel. Chlormequat chloride solo formulations may also contain choline chloride, which reduces the mammalian toxicity of chlormequat, and examples of trade names are 5C or Cycocel 5C. Chlormequat chloride may be co-formulated with other plant growth regulators, *e.g.* mepiquat chloride, imazaquin or ethephon. Examples of trade names of co-formulated products are Cyter, Meteor, Terpal C, Mondium, Sypex. These formulations are registered and sold many countries throughout the world.

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests) is a full CIPAC method (CIPAC, 1998). Chlormequat is determined by ion chromatography on a silica-based cation exchange column using an acetone/water/ ethylenediamine/oxalic acid mixture as eluent, conductivity detector and external standardization.

The method for determination of 1,2-dichloroethane impurity involves addition of dimethylacetamide, then determination of the impurity in the headspace by capillary gas chromatography, using a fused silica capillary column with flame ionization detection. Quantification is by standard addition. The method was peer validated at 10-200 mg 1,2-dichloroethane/kg chlormequat chloride (BASF method M91/29e).

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD, EU or US-EPA, while those for the formulations were CIPAC (pH range, MT 75; storage stability at 0°C, MT 39; persistent foam, MT 47; dilution stability, MT 41; all CIPAC, 1995; and accelerated storage stability, MT 46.3, CIPAC, 2000), 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 Manual (FAO/WHO, 2002).

Containers and packaging

No special requirements for containers and packaging were identified.

Expression of the active ingredient

The active ingredient content is expressed as chlormequat chloride, in g/kg or g/l at 20°C.

Appraisal

The Meeting considered data on chlormequat chloride in support of new FAO specifications for TK and SL. The data submitted were in accordance with the requirements of the FAO/WHO Manual (FAO/WHO 2002) and supported the draft specifications, which were provided by BASF Aktiengesellschaft, NUFARM GmbH & Co KG, Ciba Speciality Chemicals and Taminco n.v. (CCC Task Force).

Chlormequat (the cation) is manufactured in the form of its chloride salt and, although the activity is derived from the cation, in the specifications the salt is considered to be the active ingredient.

Chlormequat chloride is a very hygroscopic solid and, for this reason, a TC is not manufactured commercially. The salt has a melting point of 236^{o}C (with decomposition), it is of low volatility (vapour pressure < 1 x 10^{-6} Pa at 20^{o}C, extrapolated) and very soluble in water (solubility >500 g/l at 20^{o}C at pH 4, 7 and 9). It is not lipophilic, having no tendency for bioaccumulation (log P_{ow} -3 at pH 4, 7 and 9). It is stable to hydrolysis (DT_{50} >1 year at 25^{o}C at pH 4, pH 7 and pH 9) and direct photolysis in water is not a major route of degradation (half-life 201d at 20^{o}C and pH 5.4). The main formulation type of chlormequat chloride is soluble concentrate (SL).

The Meeting was provided with commercially confidential information on the manufacturing process and batch analysis data on all impurities present at or above 1 g/kg, as well as on one impurity present below 1 g/kg, provided by members of the CCC Task Force. Mass balances were 99.2-102.1%. The Meeting agreed that the reference profile of purity and impurities should be that of BASF. These data were identical to those submitted for registration in Germany (Biologische Bundesanstalt für Land- und Forstwirtschaft, BBA). On the basis of the batch analytical data and manufacturing specifications, the Meeting agreed the materials produced by the other manufacturers of the CCC Task Force should be considered equivalent to that of BASF.

The meeting agreed that 1,2-dichloroethane is a relevant impurity and accepted both the limit and basis proposed of 0.1 g dichloroethane per kg of chlormequat chloride.

Chlormequat chloride is of moderate acute toxicity by both oral and dermal administration but it is not an irritant to eye or skin, nor a skin sensitizer. Long-term studies indicated no special target organ. Repeated oral administration resulted in diarrhoea, vomiting and salivation (dog), reduced body weight (rat), or down-growth in the ovaries (mouse) and endometrial hyperplasia (mouse). Chlormequat chloride may be formulated with choline chloride, to reduce the mammalian toxicity of the chlormequat by acting as an antidote.

Chlormequat chloride was not carcinogenic in long-term studies in rats and mice after administration via the diet. Chlormequat chloride did not lead to malformations in rats and rabbit. There were no indications of any impairment of fertility in animal studies.

The genotoxic potential of chlormequat chloride was tested covering the endpoints gene mutation, chromosome damage as well as DNA damage and repair. The *in vitro* system of human lymphocytes, as well as the *in vivo* studies performed with mice and rats, gave no indication of chromosome aberration. No DNA damage and repair were observed. Chlormequat chloride was thus devoid of mutagenic activity on the basis of the studies performed.

The ecotoxicological effects of chlormequat chloride were investigated using various organisms from major ecotoxicological groups. The results demonstrated that chlormequat chloride is of low toxicity to a broad range of aquatic and terrestrial organisms including fish, algae, birds and terrestrial invertebrates. Chlormequat chloride is of moderate toxicity only towards aquatic invertebrates (*Daphnia*).

Chlormequat was evaluated by the FAO/WHO JMPR in 1970, 1972, 1994 and 1997. The JMPR concluded that it is of moderate acute oral and dermal toxicity (LD_{50} = 200-1000 mg/kg bw), with rabbits and dogs being the most sensitive species (LD_{50} = 50-80 mg/kg bw). The JMPR also concluded that it is not carcinogenic, teratogenic, genotoxic or irritating to the eye and skin, and does not cause delayed hypersensitivity. The JMPR allocated an ADI of 0-0.05 mg/kg, based on the one-year study of toxicity in dogs as most sensitive species.

The WHO hazard classification of chlormequat chloride is: slightly hazardous.

The analytical method for determination of chlormequat cation (including identity tests for the cation) is a full CIPAC method, in which chlormequat is determined by ion chromatography with a conductivity detector and external standardisation. The identification of the active ingredient as the chloride salt of chlormequat is determined by precipitation of white silver chloride upon addition of silver nitrate solution. For the determination of the relevant impurity 1,2-dichloroethane a peer validated method was provided.

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

Recommendations

The Meeting recommended that the draft specifications (as amended) for chlormequat chloride TK and SL, proposed by CCC Task Force (BASF Aktiengesellschaft, Nufarm GmbH & Co KG, Ciba Speciality Chemicals, Taminco n.v.), should be adopted by FAO.

References

Pesticide Manual,1997	The Pesticide Manual, 11th Edition, British Crop Protection Council, 1997, UK.
CIPAC, 1995	Various MT methods, CIPAC Handbook F, Black Bear Press Ltd. 1995, UK.
CIPAC, 1998	Chlormequat chloride, pp. 77-80, CIPAC Handbook H, Black Bear Press Ltd. 1998, UK.
CIPAC, 2000	MT 46.3, p. 128, CIPAC Handbook J, Black Bear Press Ltd. 2000, UK.
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JMPR 1997 — Pesticide residues in food – 1997. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and Environment and the WHO Core Assessment Group on Pesticide Residues, Lyon, France, 1997. FAO plant production and protection paper 145, FAO, Rome, 1998.

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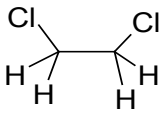
WHO 2002 — The WHO recommended classification of pesticides by hazard and guidelines to classification 2000-2002. WHO, Geneva, 2002.

Determination of 1,2-dichloroethane in aqueous solutions of chlormequat chloride

Chemical structure



Empirical Formula $C_2H_4Cl_2$

RMM 98.97

Sampling

Take at least 250 ml.

Identity test

Use the GC method below. The retention times of 1,2-dichloroethane in the sample solution and from the added calibration solution should be identical.

Outline of method

Chlormequat chloride technical concentrate or formulation is dissolved in water/dimethylacetamide and analyzed by headspace gas chromatography, using a fused silica capillary coated with polyethylene glycol. Alternatively, the chromatography can be carried out using a polydimethylsiloxane-coated capillary column. Detection is by flame ionization detector and quantification is by standard addition. Calibration by standard addition can provide excellent accuracy in headspace analysis but the quantities of sample, water and dimethylacetamide must be consistent between the sample and calibration determinations.

Reagents

Water, drinking water.

N,N-dimethyl acetamide (DMAA). purity 99.99% (w/w).

1,2-dichloroethane, at least 99.8 area % (GC) purity. Prepare a stock standard solution of 1,2-dichloroethane by weighing approximately 1 g (to the nearest 0.1 mg) into a 20 ml volumetric flask, making to volume with DMAA and mixing thoroughly. The stock standard contains 500 µg 1,2-dichloroethane per 10 µl. Aliquots should be diluted to form working standard solutions, required for the preparation of calibration solutions, to give the appropriate numbers of µg per 10 µl. If tightly stoppered, the stock and working standards may be stored in a refrigerator for up to one month, before replacing them. Stored solutions must be brought to room temperature and mixed before use.

Calibration solutions. Calibration solutions are prepared from aliquots of the sample to be analyzed and are therefore intended to calibrate only that sample. Prepare two calibration solutions, each containing different concentrations of 1,2-dichloroethane. Weigh approximately 1 g (to the nearest 0.1 mg) of the TK or SL sample into a headspace vial, add 1 ml water and exactly 10 µl of an appropriate working standard of 1,2-dichloroethane in DMAA (see preceding and following paragraphs). Immediately seal the vial with a gas tight septum.

The quantity of 1,2-dichloroethane added to the sample to form a calibration solution should be adjusted according to the concentration of chlormequat chloride in the sample and the consequent concentration of 1,2-dichloroethane represented by the specification limit. A reasonable indication of impurity concentration may be

obtained when the two levels of addition are within approximately 0.2 to 5 times the level originally present in the sample and, for checking compliance, it should be assumed that the sample contains impurity at the limit. For example, if an SL contains chlormequat chloride at 500 g/kg, the limit for 1,2-dichloroethane corresponds to 50 µg in a 1 g sample. The two calibration standards are therefore prepared by: (i) by diluting 1ml stock standard to 50 ml with DMAA (= 10 µg/10 µl); and (ii) by diluting 5ml stock standard to 10 ml with DMAA (= 250 µg/10 µl). If better accuracy is required, three calibration standards should be prepared by addition of 1,2-dichloroethane at approximately 0.5, 1 and 2 times the measured level in the sample.

Apparatus

Capillary gas chromatograph, with flame ionisation detector (FID), automatic headspace sample dispenser system, data system for signal capture and integration.

Chromatography column, fused silica. Either 50 m x 0.32 mm with 1.2 µm film thickness of polyethylene glycol (method A), or 30 m x 0.25 mm with 1.0 µm film thickness of polydimethylsiloxane (method B).

Headspace vials, 22 ml volume.

Procedure

(a) Preparation of sample solution. Weigh (to the nearest 0.1 mg) in duplicate 1 g sample solution into a headspace vial, immediately add 1ml water and 10 µl *N,N*-dimethyl acetamide (DMAA) and seal the vial with a gas tight septum.

(b) Chromatographic conditions (typical)

Method A (polyethylene glycol stationary phase)

Headspace parameters:	
Thermal equilibrium time:	45 min
Temperature during equilibrium:	70°C
Temperature of transfer line:	150°C
Pressure build-up time:	60 s
Headspace pressure:	0.9 bar
Injection time:	6 s
Dwell time:	12 s
GC conditions:	
Detector temperature:	250°C
Column oven:	50°C, 5 min isothermal 50°C to 200°C at 5°C/min 200°C, 15 min isothermal
Carrier gas:	He
Column head pressure:	0.9 bar
Split:	7ml/min
Combustion gases for FID:	hydrogen and synthetic air adjusted to the equipment manufacturer's specification.

Method B (polydimethylsiloxane stationary phase)

Headspace parameters:	
Thermal equilibrium time:	45 min
Temperature during equilibrium:	70°C
Temperature of transfer line:	150°C
Pressure build-up time:	60 s
Headspace pressure:	0.7 bar
Injection time:	12 s
Dwell time:	12 s

GC conditions:	
Detector temperature:	250°C
Column oven:	40°C, 5 min isothermal 40°C to 230°C , 5°C/min 230°C, 10 min isothermal
Carrier gas:	He
Column head pressure:	0.7 bar
Split:	11 ml/min
Combustion gases for FID:	hydrogen and synthetic air adjusted to the equipment manufacturer's specification.

(c) Repeatability and linearity checks. Inject headspace from each calibration solution at least twice and determine the mean peak area to mass ratios. The single values should differ by less than 0.5% from the mean value for each calibration solution, otherwise repeat the calibration.

If an acceptable response is obtained from the low level calibration and the mean peak area to mass ratio obtained from the highest level calibration solution is less than 99% that of the lowest level calibration solution, the quantity injected has probably exceeded the linear range of the detector. The weighings and/or dilutions must be adjusted to ensure that concentrations are within the linear range.

(d) Determination. Inject headspace from each sample solution in duplicate and "bracket" duplicate sample headspace injections by duplicate injections of the headspace from calibration solutions as follows: calibration solution 1 (two injections), sample solution 1 (two injections), calibration solution 2 (two injections).

If required, a series of four injections, representing two samples, may be made between the bracketing calibration injections but, in this case, the two samples must be of a similar product. Where dissimilar products are to be analyzed, they must be calibrated separately and injected as separate sequences.

Measure areas of the peaks obtained from 1,2-dichloroethane.

(e) Calculations

Calculate the average headspace response factor (f^{hs}) for each calibration solution as follows.

$$f^{hs} = \frac{B - A}{C}$$

where: A = average peak area of 1,2-dichloroethane in the sample without addition of dichloromethane;
B = average peak area of 1,2-dichloroethane in the calibration solution with addition of dichloromethane;
C = mass of 1,2-dichloroethane added to 1 g of sample (µg).

Calculate the overall average headspace response factor ($f^{hs)}$ obtained from the two (or three) standards used to calibrate the bracketed sample injections and use this value to calculate the 1,2-dichloroethane content of the sample(s) as follows.

$$\text{1,2-dichloroethane content (µg/g)} = \frac{A}{f^{hs}}$$

where: A = average peak area of 1,2-dichloroethane in the sample without addition of dichloromethane;
f^{hs} = overall average headspace response factor for 1,2-dichloroethane.

Calculate the concentration of 1,2-dichloroethane relative to chlormequat chloride content as follows.

$$\text{1,2-dichloroethane (g/kg of chlormequat chloride)} = \frac{\text{1,2-dichloroethane content (µg/g)}}{\text{chlormequat content (g/kg)}}$$

Repeatability, r (from manufacturer's data)

Method A, r = 0.058 mg/kg at 2.77 mg/kg 1,2-dichloroethane;
Method B, r = 0.059 mg/kg at 3.68 mg/kg 1,2-dichlorethane.

Limit of quantification (1, 2-dichloroethane in 1 g sample)

Methods A and B, 0.2 µg/g.