

**FAO SPECIFICATIONS AND EVALUATIONS
FOR AGRICULTURAL PESTICIDES**

PARAQUAT DICHLORIDE

1,1'-dimethyl-4,4'-bipyridinium dichloride

2003



FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

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Disclaimer¹

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 be 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.

Additionally, FAO wishes to alert users to the fact that improper storage, handling, preparation and/or use of pesticides can result in either a lowering or complete loss of safety and/or efficacy.

FAO is not responsible, and does not accept any liability, for the testing of pesticides for compliance with the specifications, nor for any methods recommended and/or used for testing compliance. As a result, FAO does not in any way warrant or represent that any pesticide claimed to comply with a FAO specification actually does so.

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** 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 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.

* Footnote: The publications are available on Internet under (<http://www.fao.org/AG/AGP/AGPP/Pesticid/>) or as hardcopy from the Plant Protection Information Officer.

PART ONE
SPECIFICATIONS

PARAQUAT DICHLORIDE

PARAQUAT DICHLORIDE INFORMATION

PARAQUAT DICHLORIDE TECHNICAL CONCENTRATES

FAO SPECIFICATIONS AND EVALUATIONS FOR
AGRICULTURAL PESTICIDES

PARAQUAT DICHLORIDE

INFORMATION

Common name (dication):

paraquat (E-ISO, (m)F-ISO, BSI, ANSI, WSSA, JMAF)

Synonyms:

methyl viologen

Chemical names:

dication -

IUPAC, 1,1'-dimethyl-4,4'-bipyridinium¹

CA, 1,1'-dimethyl-4,4'-bipyridinium

dichloride -

IUPAC, 1,1'-dimethyl-4,4'-bipyridinium dichloride¹

CA, 1,1'-dimethyl-4,4'-bipyridinium dichloride

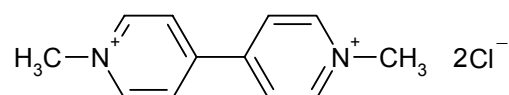
CAS No:

1910-42-5 (dichloride); 4685-14-7 (dication)

CIPAC No:

56 (dication); 56.302 (dichloride)

Structural formula (dichloride):



Molecular formula:

C₁₂H₁₄Cl₂N₂ (dichloride); C₁₂H₁₄N₂ (dication)

Relative molecular mass:

257.2 (dichloride); 186.3 (dication)

Identity tests (CIPAC G 56/SL/M-):

HPLC retention time; UV spectrum; addition of alkaline sodium dithionite to a dilute solution, where a blue colour indicates the presence of paraquat. The presence of the dichloride salt is tested with silver nitrate solution.

¹ The IUPAC name for the bipyridinium moiety is alternatively expressed as “bipyridinedium” or “bipyridilium”.

PARAQUAT DICHLORIDE TECHNICAL CONCENTRATE

FAO Specification 56.302/TK (2003)

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 reports (56.302/2003). It should be applicable to relevant products of this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specifications. The specification may not be appropriate for the products of other manufacturers. The evaluation reports (56.302/2003) as PART TWO forms an integral part of this publication.

1 Description

The material shall consist of paraquat dichloride, together with related manufacturing impurities, in the form of an aqueous solution, free from visible extraneous matter, and must contain an effective emetic (Note 1). The material may also include colorants and olefactory alerting agents.

2 Active ingredient

2.1 Identity tests (56/SL/M/2, CIPAC G, p.128)

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 Paraquat dichloride content (56/SL/M/3, CIPAC E, p.167)

The paraquat dichloride content (Note 2) shall be declared (not less than 500 g/l at 20 ± 2°C, Note 3) and, when determined, the average measured content shall not differ from that declared by more than ± 25 g/l.

3 Relevant impurities

3.1 Free 4,4'-bipyridyl (56/13/M/7.4, CIPAC 1A, p.1317)

Maximum: 1.0 g/kg (1000 ppm).

3.2 Total terpyridines (Note 4)

Maximum: 0.001 g/kg (1.0 ppm).

4 Physical properties

4.1 pH range (MT 75.3, CIPAC J, p. 131) (Note 5)

pH range: 2.0 to 6.0.

Note 1 An effective emetic, having the following characteristics, must be incorporated into the TK.


- It must be rapidly absorbed (more rapidly than paraquat) and be quick acting. Emesis must occur in about half an hour in at least 50% of cases.

- It must be an effective (strong) stimulant of the emetic centre of the brain, to produce effective emesis. The emetic effect should have a limited 'action period', of about two to three hours, to allow effective treatment of poisoning.
 - It must act centrally on the emetic centre in the brain.
 - It must not be a gastric irritant because, as paraquat is itself an irritant, this could potentiate the toxicity of paraquat.
 - It must be toxicologically acceptable. It must have a short half-life in the body (to comply with the need for a limited action period).
 - It must be compatible with, and stable in, the paraquat formulation and not affect the herbicidal efficacy or occupational use of the product.

To date, the only compound found to meet these requirements is 2-amino-4,5-dihydro-6-methyl-4-propyl-s-triazole-(1,5a)pyrimidin-5-one (PP796).

PP796 must be present in the TK at not less than 0.8 g/l.


The method for determination of [PP796](#) content is available from the Plant Protection Officer, FAO Plant Production and Protection Division.

Click here to download pdf version of **PP796** 

Note 2 To obtain the paraquat dichloride content, multiply the paraquat ion content (as determined by CIPAC method 56/SL/M/3) by 1.38.

Note 3 The lower limit of 500 g/l corresponds nominally to 442 g/kg and thus the tolerance of ± 25 g/l corresponds to $\pm 5\%$ on a g/kg basis. If, in a particular case, the declared concentration exceeds 566 g/l (>500 g/kg), the tolerance shall be ± 25 g/kg, not ± 25 g/l (± 22 g/kg). If the buyer requires specification of both g/l at 20°C and g/kg, then in case of dispute the analytical results shall be calculated as g/kg.

Note 4 **The method for [determination of total terpyridines](#) content is available from the Plant Protection Officer, FAO Plant Production and Protection Division.**

Click here to download pdf version of Method for **determination of total terpyridines** 

Note 5 The product must not be allowed to come into direct contact with metal. Containers may be manufactured from suitable polymeric materials or metal and must comply with pertinent national and international transport and safety regulations. If metal is used, containers must be lined with suitable polymeric material, or the internal surfaces treated to prevent corrosion of the container and/or deterioration of the contents.

PART TWO

EVALUATION REPORTS

PARAQUAT

2003 FAO/WHO evaluation report based on submission of data from Syngenta, UK (TC, SL, SG).

FAO SPECIFICATIONS FOR AGRICULTURAL PESTICIDES

FAO EVALUATION REPORT 56.302/2003

PARAQUAT

Explanation

The data for paraquat dichloride were evaluated in support of a review of existing FAO specifications (AGP:CP/344, Rome, 1996).

Paraquat dichloride is not under patent.

Paraquat was reviewed by the World Health Organization (WHO) and the United Nations Environment Programme (UNEP) in 1983, resulting in the publication of Environmental Health Criteria 39 (WHO, 1984), and by the International Programme on Chemical Safety (IPCS, 1991), resulting in IPCS Health & Safety Guide No 51. Paraquat was reviewed by the FAO/WHO Joint Meeting on Pesticide Residues (JMPR) in 1986 and was scheduled for periodic re-evaluation in 2003. It has been evaluated by US EPA (USEPA, 1996) and is currently under evaluation by the European Commission.

The draft specification and the supporting data were provided by Syngenta Crop Protection AG, in 2002.

Uses

Paraquat dichloride is a non-selective contact herbicide, which is absorbed by foliage, with some translocation in the xylem. It is used in broad-spectrum control of broad-leaved weeds and grasses, in a wide range of agricultural applications, for general weed control on non-crop land and also for pasture restoration.

Identity

Common name (dication):

paraquat (E-ISO, (m)F-ISO, BSI, ANSI, WSSA, JMAF)

Synonyms:

methyl viologen

Chemical names:

dication -

IUPAC, 1,1'-dimethyl-4,4'-bipyridinium¹

CA, 1,1'-dimethyl-4,4'-bipyridinium

dichloride -

IUPAC, 1,1'-dimethyl-4,4'-bipyridinium dichloride¹

CA, 1,1'-dimethyl-4,4'-bipyridinium dichloride

CAS No:

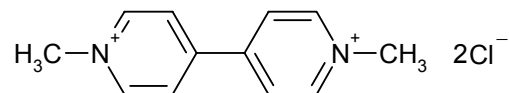
1910-42-5 (dichloride); 4685-14-7 (dication)

¹ The IUPAC name for the bipyridinium moiety is alternatively expressed as "bipyridinedium" or "bipyridilium".

CIPAC No:

56 (dication); 56.302 (dichloride)

Structural formula (dichloride):



Molecular formula:

$C_{12}H_{14}Cl_2N_2$ (dichloride); $C_{12}H_{14}N_2$ (dication)

Relative molecular mass:

257.2 (dichloride); 186.3 (dication)

Identity tests (CIPAC G 56/SL/M-):

HPLC retention time; UV spectrum; addition of alkaline sodium dithionite to a dilute solution, where a blue colour indicates the presence of paraquat. The presence of the dichloride salt is tested with silver nitrate solution.

Physicochemical properties

Table 1. Physicochemical properties of pure paraquat dichloride

Parameter	Value(s) and conditions	Purity %	Method reference
Vapour pressure	$\ll 1 \times 10^{-8}$ kPa at 25°C (extrapolated)	99.5%	OECD 104
Melting point, boiling point and/or temperature of decomposition	Melting point: >400°C Boiling point: not applicable Decomposition temperature: 340°C	99.5%	OECD 102
Solubility in water	620g/l at 20 °C across pH range	99.5%	OECD 105 (flask method)
Octanol/water partition coefficient	$\log P_{ow} = -4.5$ at 20°C	99.5%	OECD 107 (flask method)
Hydrolysis characteristics	Paraquat dichloride is hydrolytically stable under acidic, neutral and alkaline conditions, no significant decrease in concentration having been recorded at pH 5, 7 and 9 after 30 days at 25°C and 40°C.	Not stated	Analysis of sterile aqueous buffer solutions containing known amounts of paraquat dichloride before and after storage.
Photolysis characteristics	The environmental half-life of paraquat dichloride in water under mid-European conditions was calculated to be between 2 and 820 years, depending upon seasonal sunlight and depth of water.	99.7%	Measurement of molar extinction coefficients and quantum yield, then these data used in the Frank and Klöpffer model to obtain an estimate of half-life.
Dissociation characteristics	In aqueous solution the paraquat dichloride is completely dissociated.	Not applicable	

Table 2. Chemical composition and properties of paraquat dichloride (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 98.1-99.3% and percentages of unknowns were 1.9-0.7%.
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Declared minimum paraquat dichloride content	500 g/l (442 g/kg).
Relevant impurities \geq 1 g/kg and maximum limits for them	4,4 bipyridyl, 1 g/kg (1000 ppm).
Relevant impurities < 1 g/kg and maximum limits for them	Total terpyridines 0.001 g/kg (1.0 ppm)
Stabilisers or other additives and maximum limits for them	An effective emetic (reference to effective emetic criteria) – see below. PP796, 2-amino-4,5-dihydro-6-methyl-4-propyl-s-triazole-[1,5-a]pyrimidin-5-one is the only emetic known to meet these effective emetic criteria. If PP796 is the effective emetic employed, it must be present at a minimum level of 0.23% by weight of the paraquat ion content[0.17% on a paraquat dichloride basis]
Melting or boiling temperature range	340°C, at which decomposition occurs

Criteria for effective emesis.

- ◆ The emetic must be rapidly absorbed (more rapidly than paraquat) and be quick acting. Emesis must occur in about half an hour in at least 50% of cases.
- ◆ The emetic must be an effective (strong) stimulant of the emetic centre, to produce effective emesis. The emetic effect should have a limited “action period” of about two to three hours, to allow effective treatment of poisoning.
- ◆ The emetic must be act centrally on the emetic centre in the brain.
- ◆ The emetic must be not be a gastric irritant because, as paraquat is itself an irritant, this could potentiate the toxicity of paraquat.
- ◆ The emetic must be toxicologically acceptable. It must have a short half-life in the body (to comply with the need for a limited action period).
- ◆ The emetic must be compatible with, and stable in, the paraquat formulation and not affect the herbicidal efficacy or occupational use of the product.

Toxicological summaries

Notes.

- (i) The proposer confirmed that the toxicological and ecotoxicological data included in the summary below were derived from paraquat dichloride 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 paraquat dichloride TK, based on acute toxicity, irritation and sensitization.

Species	Test	Duration and conditions or guideline adopted	Result (paraquat dichloride technical / paraquat cation).
Rat, Alpk:ApfSD, male	oral	OECD 401, 14 day observation	MLD = 344 [246 – 457] mg paraquat dichloride technical / kg bw, equivalent to 113.5 mg/kg bw expressed as paraquat cation.
Rat, Alpk:ApfSD, female	oral	OECD 401, 14 day observation	MLD = 283 [182 – 469] mg paraquat dichloride technical / kg bw, equivalent to 93.4 mg/kg bw expressed as paraquat cation.
Rat, Alpk:ApfSD, male and female	dermal	OECD 402, 24 hour, occluded, 14 day observation	MLD = >2000 mg paraquat dichloride technical / kg bw equivalent to >660 mg/kg bw expressed as paraquat cation.

Species	Test	Duration and conditions or guideline adopted	Result (paraquat dichloride technical / paraquat cation).
Rat, Alpk:Ap, male and female	inhalation	OECD 403, 4 hour nose only*, 14 day observation	LC ₅₀ = 0.83 – 1.93 mg/m ³ expressed as paraquat cation.
Rabbit, New Zealand White, female	skin irritation	OECD 404, 4 hour, occluded, 34 day, observation	Slight but persistent skin irritant.
Rabbit, New Zealand White, female	eye irritation	OECD 405, 28 day observation	Persistent, moderate to severe irritant to the rabbit eye [Class 5 on a 1-8 scale].
Guinea pigs, Dunkin Hartley, female	skin sensitization	OECD 406, Magnusson and Kligman maximization test, 24 hour, occluded, 48 hour observation	Negative, not a skin sensitizer.

* Paraquat dichloride is non-volatile and formulations containing paraquat are not applied through equipment which will generate a significant proportion (>1% w/w) of spray droplets of diameter less than 50 µm. Therefore, respirable vapour or droplets of paraquat dichloride will not be produced in practice and these toxicity data are not relevant to assessment of human risks.

Table 4. Toxicology profile of paraquat TK, based on repeated administration (sub-acute to chronic).

Species	Test	Duration and conditions or guideline adopted	Result
Rabbit, New Zealand White, male and female	Short-term dermal toxicity	21-day dermal toxicity	NOEL = 1.57 mg paraquat dichloride/kg bw/day equivalent to 1.15 mg/kg bw/day, expressed as paraquat cation. LOEL = 3.61 mg paraquat dichloride /kg bw/day, equivalent to 2.6 mg/kg bw/day, expressed as paraquat ion.
Mouse, ICR-CRJ SPF, male and female	Short-term toxicity	13-week dietary	NOEL = 100 ppm, equivalent to approximately 12 and 14 mg/kg bw/day, expressed as paraquat ion in males and females, respectively. LOEL = 300 ppm, equivalent to approximately 36 and 42 mg/kg bw/day, expressed as paraquat ion in males and females, respectively.
Rat, Fischer CDF (F344), male and female	Short-term toxicity	13-week dietary	NOEL = 100 ppm, equivalent to approximately 6 and 7 mg/kg bw/day, expressed as paraquat ion in males and females, respectively. LOEL = 300 ppm, equivalent to approximately 20 and 21 mg/kg bw/day, expressed as paraquat ion in males and females, respectively.
Dog, Beagle, male and female	Short-term toxicity	13-week dietary	NOEL = 20 ppm, equivalent to approximately 0.6 and 0.7 mg/kg bw/day, expressed as paraquat ion in males and females, respectively. LOEL = 60 ppm, equivalent to approximately 2 mg/kg bw/day, expressed as paraquat ion in males and females.

Species	Test	Duration and conditions or guideline adopted	Result
Dog, Beagle, male and female	Short-term toxicity	1-year dietary	NOEL = 15 ppm, equivalent to approximately 0.45 and 0.48 mg/kg bw/day, expressed as paraquat ion in males and females, respectively. LOEL = 30 ppm, equivalent to approximately 0.9 and 1.0 mg/kg bw/day, expressed as paraquat ion in males and females, respectively.
Mouse, Alpk Swiss-derived, male and female	Carcinogenicity	99-week dietary	Not tumorigenic. NOAEL = 12.5 ppm, equivalent to approximately 1.5 mg/kg bw/day, expressed as paraquat ion in males. NOEL = 37.5 ppm, equivalent to approximately 4.3 mg/kg bw/day, expressed as paraquat ion in females.
Rat, Fischer 344, male and female	Chronic toxicity / carcinogenicity	113-117 weeks for males and 122-124 weeks for females	Not carcinogenic. NOEL = 25 ppm, equivalent to approximately 1.25 mg/kg bw/day, expressed as paraquat ion. LOEL = 75 ppm, equivalent to approximately 3.75 mg/kg bw/day, expressed as paraquat ion.
Rat, Alpk:APfSD, male and female	Reproductive toxicity	3-generation, 2 litters per generation	No effect on reproductive parameters. NOEL for toxicity = 25 ppm, equivalent to approximately 2.3 mg/kg bw/day, expressed as paraquat ion. NOEL for reproductive effects = >150 ppm, equivalent to approximately 13 mg/kg bw/day, expressed as paraquat ion.
Mice, CrI:CD1 (ICR) BR, female	Developmental toxicity	Gavage	NOEL for both maternal and developmental toxicity = 15 mg/kg bw/day expressed as paraquat ion.
Mice, Alpk SPF, female	Developmental toxicity	Gavage	Not teratogenic. No significant influence on embryonic or foetal development. NOEL for developmental toxicity = >10 mg/kg bw/day expressed as paraquat ion.
Rat, Alpk:SPF, female	Developmental toxicity	Gavage	Not teratogenic. NOEL for maternal and developmental toxicity > 1mg/kg bw/day expressed as paraquat ion.
Rat, Alpk:APfSD	Developmental toxicity	Gavage	Not teratogenic. NOAEL for maternal and developmental toxicity = 3 mg/kg bw/day expressed as paraquat ion.

Table 5. Mutagenicity profile of paraquat dichloride TK, based on *in vitro* and *in vivo* tests.

Species	Test	Conditions	Result
Mouse, lymphocytes (L5178Y)	OECD 476, L5178Y mouse lymphoma assay (<i>in vitro</i>)	Doses of 23 – 361 µg/ml	Negative

Species	Test	Conditions	Result
Human lymphocytes	OECD 473, Cytogenetic study (<i>in vitro</i>)	Dosed at 90, 903 and 1807 µg/ml	Positive
Chinese hamster lung fibroblasts	OECD 479, Sister chromatid exchange assay (<i>in vitro</i>)	Dosed at 0.9, 1.8, 9, 18, 90 and 177 µg/ml	Positive
Rat hepatocytes	OECD 482, DNA damage and repair/unscheduled DNA synthesis (<i>in vitro</i>)	Dosed at 0.19 ng/ml to 1.86 mg/ml	Negative
Rat somatic cells	Rat cytogenetic assay (<i>in vivo</i>)	Male and female Wistar rats given a single oral dose at 15, 75 and 150 mg/kg	Negative
Mouse somatic cells	OECD 474, Micronucleus test (<i>in vivo</i>)	Male and female C57BL/6J/Alpk mice given a single oral dose at 52 and 83 mg/kg	Negative
Rat somatic cells	UDS assay (<i>in vivo</i>)	Single oral dose at 42 to 120 mg/kg	Negative
Mouse germ cells	Dominant lethal (<i>in vivo</i>)	Male CD1 mice dosed orally at 0, 0.04, 0.4 and 4.0 mg/kg for 5 days.	Negative

Table 6. Ecotoxicology profile of paraquat dichloride TK.

Species	Test	Duration and conditions	Result
<i>Daphnia magna</i> , (water flea)	Acute toxicity	EEC Method C2, Static system, 20-21°C, 48-hour observation	24 and 48 hour EC ₅₀ = 11.8 and 4.4 mg/l, expressed as paraquat ion, respectively. 48 hour NOEC = 2.2 mg/l expressed as paraquat ion.
<i>Daphnia magna</i> , (water flea)	Chronic toxicity	21-day exposure, based on OECD Guideline 202, modified by individually separating the <i>Daphnia</i> static system, growth and reproduction monitored	NOEC = 0.12 mg/l expressed as paraquat ion.
<i>Oncorhynchus mykiss</i> , (rainbow trout)	Acute toxicity	EEC Method C1, static system at 15°C	24, 48, 72 and 96 hour LC ₅₀ = 33, 22, 22 and 19 mg/l, expressed as paraquat ion, respectively. 96 hour NOEC = <0.3 mg/l, expressed as paraquat ion
<i>Cyprinus carpio</i> , (mirror carp)	Acute toxicity	EEC Method C1, static system at 22°C	24, 48, 72 and 96 hour LC ₅₀ = >112, >112, >112 and 98 mg/l expressed as paraquat ion, respectively. 96 hour NOEC = 60 mg/l expressed as paraquat ion.

Species	Test	Duration and conditions	Result
<i>Oncorhynchus mykiss</i> , (rainbow trout)	Chronic toxicity	21-day fish juvenile growth test, based upon OECD Method 204, with the exposure period extended to 21 days. Broadly in agreement with the draft OECD guideline 'Fish, juvenile growth test - 28 days', except that the exposure was for 21 days. Flow through system at 15°C	NOEC = 8.5 mg/l expressed as paraquat ion.
<i>Selenastrum capricornutum</i> , (green alga)	Effect on growth	Based on OECD Guideline 201 but with an extension of the exposure period to 96 hours. Static system at 24°C, biomass and growth rate observed	EbC ₅₀ = 0.075 mg/l expressed as paraquat ion. ErC ₅₀ = 0.20 mg/l expressed as paraquat ion. NOEC = 0.016 mg/l expressed as paraquat ion.
<i>Eisenia foetida</i> , (earthworm)	Acute toxicity	Laboratory study in artificial soil	LC ₅₀ = >1000 mg/kg dry soil, expressed as paraquat ion
<i>Apis mellifera</i> (honey bee)	Acute oral toxicity	Based on UK data requirements for approval under the Control of Pesticides Regulations, Working Document D3 (revised 1979). Consistent with EPPO guideline 170. Controlled environment at 22°C	24, 48, 72, 96 and 120 hour LD ₅₀ = 154, 50.9, 26.3, 19.5 and 11.2 µg/bee, expressed as paraquat ion, respectively.
<i>Apis mellifera</i> (honey bee)	Acute contact toxicity	Based on UK data requirements for approval under the Control of Pesticides Regulations, Working Document D3 (revised 1979). Consistent with EPPO guideline 170. Controlled environment at 22°C	72, 96 and 120 hour LD ₅₀ = 108, 89.1 and 50.9 µg/bee, expressed as paraquat ion, respectively.
<i>Colinus virginianus</i> , (bobwhite quail)	Acute toxicity	Oral intubation in distilled water, 14 day observation	LD ₅₀ = 127 mg/kg bw expressed as paraquat ion. LLD = 115 mg/kg bw expressed as paraquat ion. NOEL = 72 mg/kg bw expressed as paraquat ion.
<i>Anas platyrhynchos</i> , (mallard duck)	Acute toxicity	Oral intubation in propylene glycol, 14 day observation	LD ₅₀ = 144 mg/kg bw expressed as paraquat ion.
<i>Colinus virginianus</i> , (bobwhite quail)	Short-term toxicity	5 days treatment, 3 days observation	LC ₅₀ = 711 mg/kg diet expressed as paraquat ion.
<i>Anas platyrhynchos</i> , (mallard duck)	Short-term toxicity	5 days treatment, 3 days observation	LC ₅₀ = 2932 mg/kg diet expressed as paraquat ion.
<i>Coturnix japonica</i> , (Japanese quail)	Short-term toxicity	5 days treatment, 3 days observation	LC ₅₀ = 703 mg/kg diet expressed as paraquat ion

Species	Test	Duration and conditions	Result
<i>Colinus virginianus</i> , (bobwhite quail)	Reproductive toxicity	18 week dietary treatment. Egg laying and collection started after 10 weeks on treated diet and lasted for 8 weeks.	NOEC for toxicity and reproduction = 100 mg/kg diet expressed as paraquat ion.
<i>Anas platyrhynchos</i> , (mallard duck)	Reproductive toxicity	18 week dietary treatment. Egg laying and collection started after 10 weeks on treated diet and lasted for 8 weeks.	NOEC for toxicity = 100 mg/kg diet expressed as paraquat ion. NOEC for reproduction = 30 mg/kg diet expressed as paraquat ion.

Paraquat dichloride was evaluated by WHO (WHO, 1984), by IPCS (IPCS, 1991) and by the FAO/WHO JMPR in 1986 (by which it is subject to a periodic re-evaluation in 2003). The IPCS (1991) review concluded that residue levels of paraquat in food and drinking-water, resulting from its normal use, are unlikely to pose a health hazard for the general population.

The WHO/PCS hazard classification (WHO 2002) of paraquat dichloride is: moderately hazardous, class II.

The US EPA concluded, from acute toxicity studies on laboratory animals, that paraquat is highly toxic by the inhalation route and was placed in Toxicity Category I (the highest of four levels) for acute inhalation effects. However, the EPA established that the large droplets arising in agricultural practice (400 to 800 µm) are well beyond the respirable range and therefore inhalation toxicity is not a toxicological endpoint of concern. Paraquat is moderately toxic (Category II) by the oral route and slightly toxic (Category III) by the dermal route. Paraquat will cause moderate to severe eye irritation and minimal dermal irritation and has been placed in Toxicity Categories II and IV for these effects (USEPA, 1997). Paraquat was classified as a "Group E" chemical, i.e. one showing evidence of non-carcinogenicity to humans. The no observed effect levels (NOEL) for maternal toxicity are equal to, or more conservative (protective) than, the NOEL based on developmental toxicity. There is no evidence that paraquat is associated with reproductive effects. Paraquat also shows no evidence of causing mutagenicity. The US EPA has determined that there is a reasonable certainty that no harm will result to infants and children or to the general population from aggregate exposure to paraquat dichloride residues. The EPA does not believe that the effects produced by paraquat would be cumulative with those of other, structurally related, compounds.

Formulations

The main formulation types available are SL and SG.

The SL formulations are registered and sold in many countries throughout the world. SG formulations are registered in Europe and sold mainly in the UK.

Methods of analysis and testing

Analytical methods for the active ingredient (including identity tests) were published in CIPAC Handbook E, pp. 75 and 167, and utilise a colorimetric procedure based on the blue free-radical ion produced by paraquat. The method(s) for determination of impurities are based on GC-FID, GC-MS and CE.

Relevant impurity, 4,4'-bipyridyl, is determined by GC-FID (CIPAC 56/13) the group of relevant impurities, the terpyridines, are determined by GC-MS.

The method for the terpyridines, relevant impurities and for the emetic have been peer evaluated only for the TK, but the peer validation for the analysis of the impurities of the formulations is still to be finalized.

Test methods for determination of physico-chemical properties of the technical active ingredient were essentially OECD methods, with CIPAC procedures being used for formulation assessment (as indicated in the specifications).

Physical properties

The physical properties, the methods for testing them and the limits proposed for the SL and SG formulations, comply with the requirements of the FAO Manual (5th edition).

Containers and packaging

Detailed requirements for containers are given in the specifications, as a note, but it is important to prevent paraquat dichloride from coming into contact with metals.

Expression of the active ingredient

The active ingredient is expressed as paraquat dichloride.

Appraisal

Data submitted were in accordance with the FAO/WHO Manual (2002, 1st edition) and supported the proposed specifications.

Paraquat dichloride specifications were previously developed under the old FAO procedure in 1994 (TK and SL) and published by FAO. Revised FAO specifications (TK and SL) and an additional specification (SG) for paraquat dichloride were proposed under the new procedure by Syngenta Crop Protection AG.

Paraquat dichloride is no longer under patent.

Paraquat dichloride is a non-selective contact herbicide, highly soluble and stable in water (pH 5-9), only very slowly subject to photolysis and essentially non-volatile. It very readily, and essentially irreversibly, binds to soils and sediments.

The proposer provided the meeting with commercially confidential information on the two manufacturing processes (a third manufacturing process was no longer in use) for paraquat dichloride and concomitant impurities. Data for five batches from each of the two manufacturing processes were provided for the TK. Addition of water and an emetic (after reactions are complete) complete the TK manufacturing process. Other safening additives, such as warning colorants, stenching agents and thickeners (for liquid formulations) are also incorporated. Mass balances were good: 99.0-99.3% characterized one manufacturing process, while 98.1-99.0% characterized the second process.

The proposer identified two relevant impurities of manufacturing (4,4'-bipyridyl and total terpyridines), both of which are normally below 0.5 g/kg. Minimum levels were specified for the emetic additive, and maximum levels for the two proposed relevant impurities, in the draft specifications for paraquat dichloride TK, SL and SG. Data submitted to FAO for TK purity, impurities and emetic content were similar to those

submitted for registration of paraquat dichloride in the UK. A difference between the two sets of data was that terpyridines were not included in the UK data, because the concentrations are well below 1 g/kg. Both the terpyridines and 4, 4' bipyridyl were below 1 g/kg in batch analysis data submitted to FAO, regardless of which of the two current manufacturing processes was employed. The proposer noted that terpyridines are highly toxic, whilst, in some respects, 4,4'-bipyridyl is rather more toxic than paraquat dichloride. WHO/PCS opinion was to accept these views. The proposed new limit of 1 g/kg for 4,4'-bipyridyl is below the level of the previous FAO Specification (56/TK/S/F-1994). The Meeting agreed that the two impurities should be considered as relevant.

The method of analysis for paraquat dichloride is based on a colorimetric procedure, in which the blue paraquat radical, formed upon addition of alkaline sodium dithionite, is measured (CIPAC Handbook E, pages 75-78 and 167-168). The presence of paraquat as the dichloride salt may be identified by a check for chloride, using silver nitrate solution.

Methods for impurities are based on GC-FID (4,4' bipyridyl, CIPAC Handbook E, p.168 and CIPAC Handbook 1A, p. 1245) or GC-MS (terpyridines). Determination of the content of emetic, PP796, is based on capillary GC. The methods for the emetic and terpyridines have undergone satisfactory peer validation for the TK but further validation is underway for analysis of the formulations.

The proposer stated that physicochemical properties of paraquat dichloride were essentially determined using OECD methods, with CIPAC procedures used for assessment of formulation characteristics, as indicated in the specifications.

Paraquat dichloride was evaluated by WHO IPCS (1983 and 1991) with a classification of moderately hazardous assigned. The acceptable daily intake estimated by the FAO/WHO JMPR is 0-0.004 mg/kg. The US EPA has assigned a Category II acute toxicity to paraquat dichloride, which indicates it is moderately toxic. However, once paraquat is ingested and absorbed in sufficient amount, poisoning is essentially irreversible, with death as the probable end-point. Thus, all paraquat products must contain an effective emetic, to reduce the risk of accidental or deliberate ingestion and absorption. Paraquat is of low dermal toxicity but the US EPA classified paraquat dichloride in its highest toxicity class, Category I, for inhalation hazard. Nonetheless, the agency noted that, because the spray droplets produced in normal agricultural uses are too large to be respirable, the inhalation risk is actually very low. Paraquat dichloride is moderately toxic to aquatic invertebrates, slightly toxic to fish, moderately toxic to avian species and relatively non-toxic to bees.

As a result of evaluation of paraquat under Directive 91/414/EEC, the European Commission is proposing to make a colorant, an effective emetic and a stenching (or other olfactory alerting) agent, mandatory requirements for paraquat formulations. The proposer recommended the revised specifications be amended to reflect these same standards. The Meeting accepted the requirements for a stenching agent and emetic in paraquat product descriptions. The Meeting also agreed that a note to the specifications should identify the only emetic currently known to be satisfactory and provide both a minimum concentration and a suitable analytical method for it. The Meeting agreed that the note on emetic content should allow for a possible alternative compound, by describing the characteristics required for an effective emetic.

Paraquat dichloride is not mutagenic and EPA placed it in Group E for chemicals showing evidence of being non-carcinogenic to humans. Further, the evidence available indicates that paraquat dichloride has no effect on reproduction parameters and is non-teratogenic.

Certain amendments were made to the draft specifications, as agreed between the Meeting and the proposer. Apart from the exceptional requirements identified in the appraisal, the specifications were in accordance with the normal requirements of the FAO/WHO Manual.

Recommendations

The meeting recommended that the specification for paraquat dichloride TK, as amended, should be adopted by FAO. The Meeting recommended that the specifications for SL and SG, as amended should be adopted by FAO, subject to satisfactory completion of peer validation of the analytical methods for terpyridines and the emetic.

References

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| WHO, 1984 | Environmental Health Criteria 39: Paraquat and diquat. World Health Organization, Geneva, 1984. |
| IPCS, 1991 | Health and Safety Guide No. 51. Paraquat Health and Safety Guide. World Health Organization, Geneva. 1991. |
| WHO, 2002 | The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 2000-2002 (WHO/PCS/01.5). World Health Organisation, Geneva, 2002. |
| USEPA, 1997 | R.E.D. Facts. Paraquat dichloride (EPA-738-F-96-018). United States Environmental Protection Agency, 1997. |
| US EPA, 1996 | Reregistration Eligibility Decision (RED), Paraquat dichloride. List A Case 0262. United States Environmental Protection Agency, 1996. |

