FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

DIQUAT DIBROMIDE[1]

1,1'-ethylene-2,2'-bipyridyldiylium dibromide

FOOD AND AGRICULTURE ORGANIZATION *of* THE UNITED NATIONS

[1] Diquat is the ISO common name for the 1,1'-ethylene-2,2'-bipyridyldiylium dication.

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DIQUAT DIBROMIDE

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, the development of FAO specifications has followed the **New Procedure**, subsequently described in the 1st edition of "Manual for Development and Use of FAO and WHO Specifications for Pesticides" (2002) and amended with the supplement of this manual (2006), 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 JMPS, rather than the JMPS.]

FAO Specifications now only apply to products for which the technical materials have been evaluated. Consequently from the year 2000 onwards the publication of FAO specifications under the **New Procedure** has changed. Every specification consists now of two parts, namely the specifications and the evaluation report(s):

Part One: **The Specification** of the technical material and the related formulations of the pesticide in accordance with chapters 4 to 9 of the "Manual on development and use of FAO and WHO specifications for 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. Dates of publication of the earlier versions, if any, are identified in a footnote. Evaluations bear the date (year) of the meeting at which the recommendations were made by the JMPS.

* NOTE: publications are available on the internet at http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/en/

PART ONE

SPECIFICATIONS

DIQUAT DIBROMIDE

DIQUAT DIBROMIDE

INFORMATION

Common name

Diquat (E-ISO, (m) F-ISO, BSI, ANSI, WSSA, JMAF). Refers to the dication, not the salt.

Synonyms

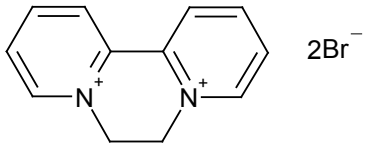
None

Chemical name

IUPAC 1,1'-ethylene-2,2'-bipyridyldiylium dibromide

CA 6,7-dihydrodipyrido[1,2-*a*:2',1'-*c*]pyrazinediium dibromide

Structural formula



Empirical formula

$C_{12}H_{12}Br_2N_2$ (dibromide)

$C_{12}H_{12}N_2$ (dication)

Relative molecular mass

344.5 (dibromide)

362.5 (dibromide monohydrate)

184.2 (dication)

CAS Registry number

85-00-7 (dibromide)

6385-62-2 (dibromide monohydrate)

2764-72-9 (dication)

CIPAC number

55.303 (dibromide)

55 (dication)

Identity tests CIPAC method 55/SL/M/2, CIPAC Handbook G, p.47, (1995)

Chemical. A green colour, following addition of alkaline sodium dithionite to a dilute aqueous solution indicates the presence of diquat.

UV spectroscopy. The UV spectrum over the range 200 to 350nm using water as a reference. The absorption maximum in the sample solution should be similar to that for the standard solution.

HPLC. Using method 55 + 56/SL/M/2.3, but omitting paraquat from the calibration solution, the relative retention time for diquat should not deviate by more than 1% from that of the calibration solution.

Semi-quantitative identity test for bromide. Capillary electrophoresis.

DIQUAT DIBROMIDE TECHNICAL CONCENTRATE (Note 1)

FAO specification 55.303/TK (February 2008*)

*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 (*55.303/2005*). It should be applicable to TK produced by 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 TK produced by other manufacturers. The evaluation report (*55.303/2005*), as PART TWO, forms an integral part of this publication.*

1 Description

The material shall consist of diquat dibromide, together with related manufacturing impurities, in the form of an aqueous solution (Note 1) and shall be free from visible extraneous matter and added modifying agents.

2 Active ingredient

2.1 **Identity tests** (55/TC/M/2, CIPAC Handbook G, p.47, 1995)

The active ingredient (diquat and bromide components, Note 2) shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 **Diquat dibromide content** (55/TC/M/3, CIPAC Handbook E, p.74, 1993)

The diquat dibromide content (Note 3) shall be declared (not less than 377 g/kg or 467 g/l at 20 ± 2ºC, Note 4) and, when determined, the average measured content shall not differ from that declared by more than ± 5%.

3 Relevant impurities

3.1 **Free 2,2'-bipyridyl** (55/13/M/7.4, CIPAC Handbook 1A, p.1245, 1980)

Maximum: 0.75 g/kg (750 ppm).

3.2 **Total terpyridines** (Note 5)

Maximum: 0.001 g/kg (1.0 ppm).

3.3 **Ethylene dibromide** (Note 6)

Maximum: 0.01 g/kg (10 ppm).

4 Physical properties

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

pH range: 3.5 to 7.5.

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* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/en/

Note 1 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.

Note 2 The method for identification of bromide in technical and formulated diquat dibromide (including mixtures with paraquat dichloride) can be downloaded here.

Note 3 To calculate the diquat dibromide content, multiply the diquat ion content (as determined by CIPAC method 55/SL/M/3) by 1.87.

Note 4 If the buyer requires specification of both g/l at 20°C and g/kg, then in cases of dispute the analytical results shall be calculated as g/kg.

Note 5 The method for determination of total terpyridines in technical and formulated diquat dibromide is available from CIPAC at http://www.cipac.org/lnpub.htm.

Note 6 The method for determination of ethylene dibromide in technical and formulated diquat dibromide can be downloaded here.

DIQUAT DIBROMIDE SOLUBLE CONCENTRATE (Notes 1 and 2)

FAO specification 55.303/SL (February 2008*)

*This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturer whose names is listed in the evaluation report (*55.303/2005*). It should be applicable to relevant products of this manufacturer, and those of any other formulators who use only TK 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 TK from other sources. The evaluation report (*55.303/2005*), as PART TWO, forms an integral part of this publication.*

1 Description

The material shall consist of technical diquat dibromide, complying with the requirements of FAO specification 55.303/TK (February 2008), in the form of an aqueous solution (Notes 1 and 2), together with any other necessary formulants. It shall contain not more than a trace of suspended matter, immiscible solvents and sediment.

2 Active ingredient

2.1 **Identity tests** (55/SL/M/2, CIPAC G, p.47, 1995)

The active ingredient (diquat and bromide components, Note 3) shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 **Diquat dibromide content** (55/SL/M/3, CIPAC E, p.74, 1993, Note 4)

The diquat dibromide content (Note 5) shall be declared (g/kg and/or g/l at 20 ± 2ºC, Note 6) and, when determined, the average content measured shall not differ from that declared by more than the following tolerances.

Declared content, g/kg or g/l at 20 ± 2ºC	Permitted tolerance
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
Note: the upper limit is included in each range.	

3 Relevant impurities

3.1 **Free 2,2'-bipyridyl** (55/13/M/7.4, CIPAC Handbook 1A, p.1245, 1980)

Maximum: 0.75 g/kg (750 ppm).

3.2 **Total terpyridines** (Note 7)

* 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/

Maximum: 0.001 g/kg (1.0 ppm).

3.3 **Ethylene dibromide** (Note 8)

Maximum: 0.01 g/kg (10 ppm).

4 Physical properties

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

pH range 4.0 to 8.0.

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

The formulation, after the stability test at 54°C (see 5.2) and following dilution (Note 9) with CIPAC standard water 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 (Note 10).

4.3 **Persistent foam** (MT 47.2, CIPAC Handbook F, p. 152, 1995) (Note 11)

Maximum: 60 ml after one minute.

5 Storage stability

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

After storage at 0 ± 2ºC 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 ± 2ºC for 14 days, the determined average active ingredient content must not be lower than 97%, relative to the determined average content found before storage (Note 12), and the product shall continue to comply with the clause for:

- pH range (4.1).

Note 1 FAO specifications 55/SL and 56/SL are applied to mixed SL formulations, containing both diquat and paraquat. An emetic is added to all formulations containing paraquat and the extra precautions required for handling solutions of paraquat must be observed when handling the mixed formulation. The method for determination of the emetic in technical and formulated paraquat was peer-validated in 2003 can be downloaded here.

Note 2 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.

Note 3 The method for identification of bromide in technical and formulated diquat dibromide (including mixtures with paraquat dichloride) can be downloaded here.

Note 4 If the SL contains both diquat and paraquat, CIPAC method 55+56/SL/M/3 (CIPAC Handbook E, p.75, 1993) should be used for determination of active ingredient content.

Note 5 To obtain the diquat dibromide content, multiply the diquat ion content (as determined by CIPAC method 56/SL/M/3) by 1.87.

Note 6 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 7 The method for determination of total terpyridines in technical and formulated diquat dibromide is available from CIPAC at http://www.cipac.org/lnpub.htm.

Note 8 The method for determination of ethylene dibromide in technical and formulated diquat dibromide can be downloaded here.

Note 9 The concentration for the test should not be higher than the highest concentration recommended for use.

Note 10 Some formulations containing additional wetter may show signs of layering and produce a trace of oily precipitate under the test conditions defined in MT 41. This is acceptable and does not affect biological efficacy or spray characteristics at normal spray dilution.

Note 11 The mass of sample used in the test should correspond to the highest concentration recommended for use.

Note 12 Samples of the product taken before and after the storage stability test should be analyzed concurrently after the test to reduce the analytical error.

PART TWO

EVALUATION REPORTS

DIQUAT

DIQUAT

FAO/WHO EVALUATION REPORT 55/2005

Recommendations

The Meeting recommended the following.

(i) All existing FAO specifications (1994 and 1973) for diquat and diquat + paraquat should be withdrawn.

(ii) The specifications for diquat dibromide TK and SL, proposed by Syngenta Crop Protection AG, as amended, should be adopted by FAO, subject to acceptable validation of the analytical method for determination of terpyridines[1].

(iii) The manufacturer should endeavour to develop and validate analytical methods which will enable the limits for relevant impurities to be expressed on the basis of active ingredient content, instead of the whole product. As and when such improved methods become available, the specified limits for relevant impurities in diquat should be reviewed accordingly.

Appraisal

The Meeting considered data on diquat, submitted by Syngenta Crop Protection AG, for review of existing FAO specifications. Existing specifications for diquat dibromide specifications were developed under the old FAO procedure in 1994 (TK, SL and mixed SL including paraquat dichloride, AGP:CP/341, 1996). In addition, 1973 FAO specifications for diquat apparently remained in force, including a specification for SG. Revised FAO specifications for the TK, SL and mixed diquat + paraquat SL were proposed. The data submitted were in accordance with FAO/WHO Manual (2002, 1st edition).

Diquat dibromide is no longer under patent.

Diquat dibromide is a non-volatile ionic, non-selective contact herbicide, highly soluble in water and stable at pH 5-7, with <10% loss of diquat observed over 30 days at pH 9. It is subject to slow photolysis. Diquat dication rapidly binds to soils, sediment and plant materials.

The proposer provided the Meeting with commercially confidential information on the manufacturing process for diquat dibromide and on manufacturing limits for impurities. Five batch analysis data were provided for the TK. Mass balances were high, 998-1007g per kg, with a declared minimum for diquat dibromide of 467 g/l (377 g/kg). These data were confirmed as similar to those submitted for registration in the UK.

No relevant impurities at ≥1 g/kg were identified in the TK but three impurities at <1 g/kg were consistently present and were proposed as relevant, due to their exceptional hazards. Their manufacturing limits in the TK were: 2,2'-bipyridyl,

[1] An LC-MS/MS method for determination of terpyridines was peer-validated and accepted by CIPAC in 2007 and is available at http://www.cipac.org/lnpub.htm.

0.75 g/kg (0.075% or 750 ppm); ethylene dibromide, 0.01 g/kg (0.001% or 10 ppm); and total terpyridines, 0.001 g/kg (0.0001% or 1 ppm). The isomeric 4,4'-bipyridyl and total terpyridines were identified in FAO paraquat specifications (2003) as relevant, on the basis of their high relative toxicity. Paraquat is about 100 times more toxic than diquat and therefore the Meeting agreed that 2,2'-bipyridyl and total terpyridines should also be designated as relevant impurities in diquat. Ethylene dibromide is a carcinogen and the Meeting agreed that it should also be designated as a relevant impurity.

Exceptionally, the proposed limits for these relevant impurities in the TK (containing a minimum of 377 g/kg diquat dibromide) and SL (including the SL plus paraquat) were based on the whole product, not the content of active ingredient. The manufacturer explained that this was unavoidable, due to limitations in the analytical methods, which are currently unable to determine lower levels of impurities in the formulations with acceptable accuracy, although they may be present at levels up to about half the proposed limits. The Meeting acknowledged that analysis and specifications for relevant impurities in paraquat formulations are subject to the same limitations. The manufacturer stated that an LC-DAD method for determination of terpyridines in both diquat and paraquat formulations had been investigated but that efforts had subsequently focused upon LC-MS/MS. Although the work was still in progress, the sensitivity of the LC-MS/MS technique offered the potential for limits in the formulations to be based on diquat dibromide content. This was welcomed by the Meeting but it was agreed that, based on currently achievable analytical performance, the limits in both TK and SL specifications should be on a whole product basis. WHO/PCS advised that the proposed limits were acceptable and the Meeting agreed.

The analytical method for determination of diquat dibromide, in which only the dication is detected, is a full CIPAC method (CIPAC Handbook G, 1995).

The semi-quantitative method for identification of bromide, in the absence (diquat TK, SL) or presence (diquat + paraquat SL) of chloride is based on capillary electrophoresis.

The method for determination of 2,2'-bipyridyl is based on CG/FID (CIPAC 55/SL/M/7.4, CIPAC A, p1245). The Meeting noted that the CIPAC method for bipyridyl employs packed-column GC, an old technology for which serviceable equipment no longer exists in most laboratories. This problem is often associated with older methods but, although it is expected that capillary GC would form an appropriate and preferable alternative in this case, a method employing this technique has not been peer-validated.

The method for determination of total terpyridines was successfully peer-validated for the analysis of paraquat TK. The manufacturer reported that extension of this GC-MS method to diquat (in the absence and presence of paraquat) had proven problematic and work was still in progress to develop and validate a robust method[1].

Ethylene dibromide is determined by capillary GC-FID and the method remained unchanged from that supplied to FAO in 1994, in support of diquat specifications

[1] An LC-MS/MS method for determination of terpyridines was peer-validated and accepted by CIPAC in 2007 and is available at http://www.cipac.org/lnpub.htm.

under the old FAO procedure. Peer validation of the method, for analysis of TK and SL (with and without paraquat) was completed in 2006.

Because all paraquat formulations must contain an effective emetic, an analytical method for the emetic PP796 in diquat + paraquat SL was peer-validated[1].

The physico-chemical properties, the methods for testing them and the limits proposed for the SL formulations complied with the requirements of the FAO/WHO manual (2002). The proposed specifications were in accordance with the requirements of the manual, with the following exceptions.

The proposed description clause in the SL specification differed from guideline given in the manual. The standard phrase: "…free from visible suspended matter and sediment…" was replaced by "…shall contain not more than a trace of suspended matter, immiscible solvents and sediments…". The proposer explained that certain batches of wetters used in current formulations result in the presence of fine oily droplets but that these do not affect the sprayability or other characteristics of the product and have not resulted in complaints from customers. The Meeting questioned whether the relevant impurities (which are non-ionic) might become concentrated within these droplets and thus create unexpected risks for the user. The proposer explained that the droplets derive from the surfactants used (a mixture of ionic and non-ionic types) and that droplet formation depends on a combination of surfactant batch and the water used. The droplets were said to be comprised mainly of the calcium salts of the ionic surfactants and the manufacturer stated that lipophilic compounds are not expected to partition into them. The Meeting accepted the modified wording of the clause.

A separate specification for diquat + paraquat SL was proposed. In general, FAO/WHO specifications are expected to apply to all products of a particular formulation type (e.g. SL), irrespective of the presence of other active ingredients. Exceptions are normally made only in cases where the ratio of active ingredients is critical for acceptable performance of the product. The exact ratio of active ingredients was not critical in this case. The proposer stated that, for the diquat + paraquat mixture, a simple diquat SL specification would not address the toxicity of paraquat and the consequent need for an emetic. The Meeting noted that anyone handling the product would only be aware that the proposed specification for a mixed formulation should be applied if the product label indicates the presence of paraquat. The existing paraquat specification incorporates appropriate handling precautions for that active ingredient. The Meeting therefore agreed that, although a separate specification for the mixed SL was not necessary, the diquat SL specification should incorporate a note, drawing attention to requirements which apply when paraquat is also present.

The Meeting noted that diquat dibromide solutions will react with many metals over a wide pH range, especially at low pH, and it was agreed that the specifications should incorporate a note to indicate that containers must be specially designed to avoid corrosion problems.

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[1] The method for determination of the emetic in technical and formulated paraquat was peer-validated in 2003 and is available from the Pesticide Management Group of the FAO Plant Protection Service or can be downloaded here.

SUPPORTING INFORMATION
FOR
EVALUATION REPORT 55/2005

Uses

Diquat dibromide is a non-selective contact herbicide, which is absorbed by foliage with some translocation in the xylem. It is active against a broad spectrum of weed species in a wide range of agricultural applications.

Identity of the active ingredient

Common name

Diquat (E-ISO, (m) F-ISO, BSI, ANSI, WSSA, JMAF). Refers to the dication, not the salt.

Synonyms

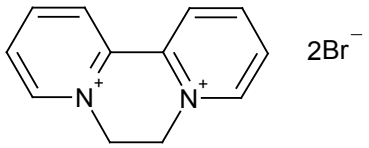
None

Chemical name

IUPAC 1,1'-ethylene-2,2'-bipyridyldiylium dibromide

CA 6,7-dihydrodipyrido[1,2-*a*:2',1'-*c*]pyrazinediium dibromide

Structural formula



Empirical formula

$C_{12}H_{12}Br_2N_2$ (dibromide)

$C_{12}H_{12}N_2$ (dication)

Relative molecular mass

344.5 (dibromide)

362.5 (dibromide monohydrate)

184.2 (dication)

CAS Registry number

85-00-7 (dibromide)

6385-62-2 (dibromide monohydrate)

2764-72-9 (dication)

CIPAC number

55.303 (dibromide)

55 (dication)

Identity tests CIPAC method 55/SL/M/2, CIPAC Handbook G, p.47, 1995.

Chemical. A green colour, following addition of alkaline sodium dithionite to a dilute aqueous solution indicates the presence of diquat.

UV spectroscopy. The UV spectrum over the range 200 to 350nm using water as a reference. The absorption maximum in the sample solution should be similar to that for the standard solution.

HPLC. Using method 55 + 56/SL/M/2.3, but omitting paraquat from the calibration solution, the relative retention time for diquat should not deviate by more than 1% from that of the calibration solution.

Semi-quantitative identity test for bromide. Capillary electrophoresis.

Physical and chemical properties

Table 1. Physicochemical properties of pure diquat dibromide

Characteristic	Value	Purity, %	Method	Reference
Vapour pressure	<<1 x 10^{-8} kPa at 25ºC.	100%	OECD 104	PP901/0024
Melting point	Decomposes before melting.	100%	OECD 102	PP901/0024
Boiling point	not applicable.			PP901/0024
Decomposition temperature	325°C.			PP901/0024
Solubility in water	718 g/l at 0°C at pH 7.2.	100%	OECD 105 (flask method)	PP901/0024
Octanol:water partition coefficient	log P K_{OW} = -4.6 at 20°C.	100%	OECD 107 (flask method)	PP901/0024
Hydrolysis	Stable under acidic, neutral and alkaline conditions. No significant decrease in concentration at pH 5 and 7, <10% decrease at pH 9 after 30days at 25ºC.	Radio-chemical purity >98% (specific activity 0.398 Gbq/mmol)	Analysis of sterile aqueous buffer solutions	PP901/0525
Photolysis	Environmental half-life of diquat dibromide in water under mid-European conditions calculated to be 2-210 days, depending on seasonal sunlight and depth of water	99.7%	Measurement of UV absorption and quantum yield, half-life estimated by Frank and Klöpffer model	PP901/0926
Dissociation characteristics	Diquat dibromide exists as the ionized salt. The diquat dication is not deprotonated at pH ≤14	-	Structural assessment	PP901/0024

Table 2. Chemical composition and properties of diquat dibromide 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 99.8–100.7% and unknowns were insignificant (total <1 g/kg).
Declared minimum diquat dibromide content in the TK	467g/l (377g/kg) as diquat dibromide
Relevant impurities ≥1 g/kg and maximum limits for them	None
Relevant impurities <1 g/kg and maximum limits for them	2,2'-bipyridyl, 0.75 g/kg (750 ppm), whole product basis ethylene dibromide, 0.01 g/kg (10 ppm), whole product basis total terpyridines: 0.001 g/kg (1 ppm), whole product basis
Stabilizers or other additives and maximum limits for them	None

Background information on toxicology/ecotoxicology

Diquat was reviewed by WHO and UNEP (WHO 1984), and by IPCS (IPCS 1991). The 1991 IPCS review concluded that residue levels of diquat in food and drinking-water, resulting from its normal use, are unlikely to pose a health hazard for the general population.

Diquat was evaluated by the FAO/WHO JMPR in 1970, 1972, 1976, 1977, 1978, 1994 and is included in the CCPR periodic review programme.

US EPA reregistered diquat in 1995 (USEPA 1995a, 1995b) and re-assessed its tolerances in 2002 (USEPA 2002). US EPA categorized diquat toxicity as follows. On the basis of slight to severe eye irritation: Toxicity Category II (2nd highest of 4 categories) for this effect. On the basis of slight acute toxicity by oral and inhalation routes: Toxicity Category II for these effects. On the basis of slight dermal irritation: Toxicity Category IV for this effect. It is not a skin sensitizer. Diquat was classified as a Group E carcinogen, that is, a chemical for which there is evidence of non-carcinogenicity for humans. US EPA determined that dietary food risks are not of concern.

Diquat was evaluated by the European Commission and included in Annex I of Directive 91/414/EEC (EU 2001).

The WHO hazard classification of diquat is: moderately hazardous, Class II (WHO 2002).

Formulations

Diquat dibromide is registered and marketed in many countries throughout the world. The main formulation type is SL and diquat may be co-formulated with paraquat.

Methods of analysis and testing

The analytical methods for diquat (including identity tests) in TC and SL are full CIPAC methods (CIPAC Handbook G, p.47, 1995). Diquat is determined by HPLC,

using UV detection at 290 nm using an internal standard. The identity test is a colorimetric procedure, based on the green diquat free radical ion.

The relevant impurities are determined by GC/FID (2,2'-bipyridyl, CIPAC 55/SL/M/-), GC/MS or LC-DAD (terpyridines), and capillary GC-FID or capillary GC-MS (ethylene dibromide). The method for total terpyridines in diquat is undergoing further development, after peer-validation studies revealed problems. The method for ethylene dibromide was successfully peer-validated in 2006. The method for determination of the emetic (PP796), added to paraquat products and present in the mixed paraquat/diquat SL, is based on reversed-phase HPLC and internal standardization with 4-nitroacetanilide. This method was also successfully peer-validated in 2006.

Analytical method(s) for determination of other impurities were based on GC-FID and CE.

Test methods for determination of physico-chemical properties of the technical active ingredient were essentially OECD methods, with CIPAC procedures being used for formulations.

Containers and packaging

It is important to prevent diquat dibromide products from coming into contact with metals. Requirements for containers are noted in the specifications.

Expression of active ingredient

The active ingredient is expressed as diquat dibromide, in g/kg or g/l at 20 ± 2ºC, which is calculated by multiplying the determined diquat dication content by 1.87.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

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

Table A. Toxicology profile of technical diquat dibromide, based on acute toxicity, irritation and sensitization (all values expressed as diquat ion)

Species	Test	Duration and conditions	Result	Reference
Rat, Alpk:ApfSD, m,f	oral	OECD 401, 14 d observation, purity 21.2% w/w	MLD = 1009 mg/kg (m), 1047 mg/kg (f), equivalent to diquat ion at 214 mg/kg (m), 222 mg/kg (f)	PP901/0079
Rat, Alpk:ApfSD, m,f	dermal	OECD 402, 24 h occluded, 14 d observation, purity 21.2% w/w	MLD >2000 mg/kg (m,f), equivalent to diquat ion at 424 mg/kg	PP901/0080
Rat, Alpk:Ap, m,f	inhalation	OECD 403, 4 h whole body, 19.5% w/w formulation, 14 d observation, purity 19.5% w/w	LC_{50} = 0.8 mg/l (m), 1.09 mg/l (f), equivalent to diquat ion at 0.121 mg/l (m), 0.132 mg/l (f)*	PP901/0161
Rabbit, New Zealand White, f	skin irritation	OECD 404, 4 h occluded, 240g/l SL formulation, 17 d observation, purity 19.9% w/w	Slight skin irritation, all signs of irritation resolved within 17 d**	PP901/1521
Rabbit, New Zealand White, f	eye irritation	OECD 405, 240g/l SL formulation, 10 d observation, purity 19.9% w/w	Mild eye irritation, all signs of irritation resolved within 10 d***	PP901/1519
Guinea pigs, Dunkin Hartley, f	skin sensitization	OECD 406, undiluted TK, 31% diquat dibromide, Magnusson & Kligman maximization test, 24 h occluded, 48 h observation, purity 26.7% w/v	Skin sensitizer****	PP901/0078 & PP901/0755

* Diquat dibromide is non-volatile and its formulations are not applied with equipment which generates a significant proportion (>1% w/w) of spray droplets <50 µm. Diquat dibromide is therefore unlikely to be inhaled and the results are not relevant to human risk assessment.

** According to European Commission Directive 2001/59/EC, classification is not required. Based on scores at 72 h, would be assigned to US EPA Category IV.

*** According to European Commission Directive 2001/59/EC, classification is not required. Positive effects cleared within 7 d, placing the material in US EPA Category III.

**** A 1 in 10 dilution would not trigger classification for sensitization.

Table B. Toxicology profile of technical diquat dibromide, based on repeated administration (sub-acute to chronic) (all values expressed as diquat ion)

Species	Test	Duration and conditions	Result	Reference
Rat, Sprague Dawley m,f	Short-term toxicity	13 week dietary, purity 20.5% w/w	NOEL = 60 ppm, equivalent to approximately 4.7 and 5 mg diquat ion/kg bw/day, m & f, respectively LOEL = 300 ppm, equivalent to approximately 23.2 and 25.3 mg diquat ion/kg bw/day, m & f, respectively	PP901/1387
Dog, Beagle, m,f	Short-term toxicity	1 year dietary, purity 26.7% w/v	NOAEL = 0.5 mg diquat ion/kg, m & f LOEL = 2.5 mg diquat ion/kg, m & f	PP901/0116
Mouse, Alpk Swiss-derived, m,f	Carcinogenicity	2 year dietary, purity 26.7% w/v	Not tumorigenic or carcinogenic NOAEL = 30ppm, equivalent to 4.2 mg diquat ion/kg bw/day, m & f LOEL = 100 ppm, equivalent to approximately 14 mg diquat ion/kg bw/day, m & f	PP901/1435
Rat, Sprague Dawley, m,f	Chronic toxicity & carcinogenicity	2 year dietary, purity 18.4% w/w	Not tumorigenic or carcinogenic NOAEL = 5 ppm, equivalent to approximately 0.2 mg diquat ion/kg bw/day, m & f LOEL = 15 ppm, equivalent to approximately 0.65 mg diquat ion/kg bw/day, m & f	PP901/0110-3
Rat, Alpk:APfSD m,f	Reproductive toxicity	2 generation, dietary, purity 26.7% w/v	No significant effect on reproductive parameters NOAEL (parental) = 16 ppm, equivalent to approximately 1.4 mg diquat ion/kg bw/day NOAEL (reproductive effects) = 240/400 ppm, equivalent to approximately 22-32 mg diquat ion/kg bw /day	PP901/0121
Rat, Alpk: APfSD, m,f	Developmental toxicity	Gavage, purity 26.2% w/v	Not teratogenic NOAEL (teratogenicity) = 40 mg diquat ion/kg NOEL (maternal and developmental toxicity) = 4 mg diquat ion/kg bw/day	PP901/0136
Rabbit, New Zealand White, m,f	Developmental toxicity	Gavage, purity 26.2% w/v	Not teratogenic NOAEL (teratogenicity) = 40 mg diquat ion/kg NOAEL (maternal toxicity) = 1 mg diquat ion/kg bw/day NOAEL (developmental toxicity) = 3 mg diquat ion/kg bw/day	PP901/0130

Table C. Mutagenicity profile of technical diquat dibromide, based on *in vitro* and *in vivo* tests (all values expressed as diquat ion)

Species	Test	Conditions	Result	Reference
S. typhimurium and *E.coli*	Bacterial gene mutation, OECD 471, *in vitro*	Doses not stated, purity 25.8% w/w	Negative ± S9, cytotoxicity at ≥100 µg/plate	PP901/0140
Mouse, lymphocytes (L5178Y)	OECD 476, mouse lymphoma assay, *in vitro*	Doses not stated, purity 25.8% w/w	Equivocal ± S9, cytotoxicity at highest concentrations	PP901/0143
Human lymphocytes	OECD 473, cytogenetic study, *in vitro*	Doses not stated, purity 53.5% w/w	Positive ± S9 but only at cytotoxic doses	PP901/0139
Mouse somatic cells	OECD 474, micronucleus test, *in vivo*	Oral doses up to 100 mg/kg, purity 25.8% w/w	Negative	PP901/0141
Rat somatic cells	Liver UDS assay, *in vivo*	Oral doses up to 900 mg/kg bw, purity 25.8% w/w	Negative. Evidence of toxicity to hepatocytes	PP901/0145
Mouse germ cells	Dominant lethal, *in vivo*	Doses up to 10 mg/kg bw/day, purity 28.6% w/v	Negative.	PP901/0137

Table D. Ecotoxicology profile of technical diquat dibromide (all values expressed as diquat ion)

Species	Test	Duration and conditions	Result	Reference
Daphnia magna, water flea	Acute toxicity	EPA-660/3-75-009, static system, 17 ± 1.5ºC, 48 h duration, purity 46.6% w/w	EC_{50} (24 h) = 2.2 mg/l EC_{50} (48 h) = 1.2 mg/	PP901/0563
Daphnia magna, water flea	Chronic toxicity	21 d exposure, based on OECD guideline 202, modified by individually separating the *Daphnia*, static system, growth and reproduction monitored, purity 27.4% w/v	NOEC = 0.125 mg/l	PP901/0566
Oncorhynchus mykiss, rainbow trout	Acute toxicity	EEC Method C1, Static system at 16ºC, purity 26.8% w/v	24, 48, 72 and 96 h LC_{50} = 69, 27, 23 and 21 mg/l, respectively 96-h NOEC = 6.7 mg/l	PP901/0970
Cyprinus carpio, mirror carp	Acute toxicity	OECD 203, static system at 23ºC, purity 26.8% w/v	24, 48, 72 and 96 h LC_{50} = 285, 143, 91 and 67 mg/l, respectively 96 hour NOEC =14 mg/l	PP901/0972

Table D. Ecotoxicology profile of technical diquat dibromide (all values expressed as diquat ion)

Species	Test	Duration and conditions	Result	Reference
Oncorhynchus mykiss, rainbow trout	Chronic toxicity	21 d, fish juvenile growth test, based on OECD Method 204, with the exposure period extended to 21 d, broadly in agreement with draft OECD guideline 'Fish, juvenile growth test - 28 days', except exposure was for 21 d; flow-through system at 15ºC, purity 26.2% w/v	NOEC = 1.4 mg/l	PP901/0559
Selenastrum capricornutum, green alga	Effect on growth	Based on OECD guideline 201 but with extension of exposure period to 96 h, static system at 24ºC, biomass and growth rate observed, purity 26.8% w/v	E_bC_{50} = 0.011 mg/l E_rC_{50} = 0.019 mg/l NOEC = 0.0068 mg/l	PP901/0572
Eisenia foetida, earthworm	Acute toxicity	Lab study in artificial soil, 200 g/l SL, based on OECD guideline 207 and EEC guideline C(L1)4, purity 20.3% w/v	14-d LC_{50} = 130 mg/kg dry soil	PP901/0556
Apis mellifera (honey bee)	Acute oral toxicity	Based on UK Data Requirements for Approval, COPR Working Document D3 (revised 1979), consistent with EPPO guideline 170, controlled environment at 24-26ºC, purity 20.1% w/v	24, 48, 72, 96 and 120 h LD_{50} = 139, 67, 23, 14 and 12 µg/bee, respectively	PP901/0542
Apis mellifera (honey bee)	Acute contact toxicity	Based on UK Data Requirements for Approval, COPR Working Document D3 (revised 1979), consistent with EPPO guideline 170, controlled environment at 24-26ºC, purity 20.1% w/v	24, 48 72, 96 and 120 h LD_{50} = 120, 77, 46, 27 and 14 µg/bee, respectively	PP901/0542
Perdix perdix, partridge	Acute toxicity	Oral intubation in distilled water, 14 d observation, USEPA guideline G 163.71-1, purity 53.7% w/w	LD_{50} = 158 mg/kg bw	PP901/0534
Anas platyrhynchos, mallard duck	Acute toxicity	Oral intubation in propylene glycol, 14 d observation, USEPA guideline G 163.71-1, purity 45.6% w/w	LD_{50} = 83 mg/kg bw	PP901/0536
Colinus virginianus, bobwhite quail	Short-term toxicity	5 d treatment, 3 d observation, similar to USEPA guideline 71-2, purity not specified	LC_{50} = 1570 mg/kg diet	PP901/1891
Anas platyrhynchos, mallard duck	Short-term toxicity	5 d treatment, 3 d observation, similar to USEPA guideline 71-2, purity not specified	LC_{50} >2677 mg/kg diet	PP901/1891

Table D. Ecotoxicology profile of technical diquat dibromide (all values expressed as diquat ion)

Species	Test	Duration and conditions	Result	Reference
Coturnix japonica, Japanese quail	Short-term toxicity	5 d treatment, 3 d observation, similar to USEPA guideline 71-2, purity not specified	LC_{50} = 721 mg/kg diet	PP901/1891
Phasianus colchicus, ring-necked pheasant	Short-term toxicity	5 d treatment, 3 d observation, similar to USEPA guideline 71-2, purity not specified	LC_{50} = 2004 mg/kg diet	PP901/1891
Colinus virginianus, bobwhite quail	Reproductive toxicity	18 week dietary, egg-laying and collection started after 10 weeks on treated diet and lasted 8 weeks; based on USEPA guideline 71-4 and OECD 206, purity 19.6% w/w	NOEC (toxicity and reproduction) = 100 mg/kg diet	PP901/0538
Anas platyrhynchos, mallard duck	Reproductive toxicity	3 weeks pre egg-laying plus 6 weeks post egg-laying exposure, dietary treatment, egg-collection lasted for 9 weeks; based on USEPA guideline 71-4, and OECD 206, purity 22.7% w/w	NOEC (reproduction) = 20 mg/kg diet	PP901/1436

Annex 2. References

Syngenta document No. or other reference	Year and title of report or publication details
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