Food and Agriculture Organization
of the United Nations

FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

DICAMBA

3,6-dichloro-2-methoxy-benzoic acid

2023

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DICAMBA

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.

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

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

INTRODUCTION

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

From 1999 onward, the development of FAO specifications follows the New Procedure, described first in the fifth edition of the "Manual on the development and use of FAO specifications for plant protection products" and later in the first edition of the “Manual on Development and Use of FAO and WHO Specifications for Pesticides” (2002) – currently available as „Manual on the development and use of FAO and WHO specifications for chemical pesticides” second edition (2022) – which is available only on the internet through the FAO and WHO web sites.

This New Procedure follows a formal and transparent evaluation process. It describes the minimum data package, the procedure and evaluation applied by FAO and the experts of the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS). [Note: prior to 2002, the experts were of the FAO Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent, which now forms part of the JMPM, rather than the JMPS.]

FAO Specifications now only apply to products for which the technical materials have been evaluated. Consequently from the year 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 the development and use of FAO and WHO specifications for chemical pesticides”.

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

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

Specifications bear the date (month and year) of publication of the current version. Evaluations bear the date (year) of the meeting at which the recommendations were made by the JMPS.

* Note: Publications are available on the internet at (https://www.fao.org/pest-and-pesticide-management/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/pesticide-specifications-list/en/) or in hardcopy from the plant protection information officer.

PART ONE

SPECIFICATIONS

DICAMBA

DICAMBA

INFORMATION

ISO common name

Dicamba (ISO 1750 (published))

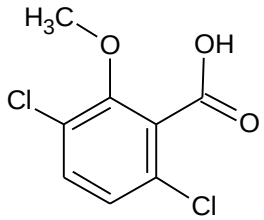
Chemical name(s)

IUPAC: 3,6-dichloro-2-methoxybenzoic acid
(or 1979 Rules: 3,6-dichloro-*o*-anisic acid)
CA: 3,6-dichloro-2-methoxybenzoic acid

Synonyms

Dicamba (BSI, ANSI, WSSA), MDBA (JMAF)

Structural formula



Molecular formula

$C_8H_6Cl_2O_3$

Relative molecular mass

221.0

266.1 (dimethylammonium salt)

259.1 (potassium salt)

243.0 (sodium salt)

CAS Registry number

1918-00-9

CIPAC number

85

Identity tests

HPLC retention time, LC-MS, IR, NMR

FAO Specification 85/TC (November 2023*)

This specification, which is PART ONE of this publication, is based on an evaluation of data submitted by the manufacturers whose names are listed in the evaluation reports (85/2001, 85/2016 & 85/2023). It should be applicable to TC produced by these manufacturers but it is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for TC produced by other manufacturers. The evaluation reports (85/2001, 85/2016 & 85/2023), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of dicamba, together with related manufacturing impurities, in the form of grey to tan coloured lumps, flakes, granules or powder, free from visible extraneous matter and added modifying agents.

2 Active Ingredient

2.1 **Identity tests** (CIPAC 85/TC/M/2, Handbook K, p. 33, 2003)

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 **Dicamba content** (CIPAC 85/TC/M/3, Handbook K, p. 33, 2003)

The dicamba content shall be declared (not less than 850 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

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* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: https://www.fao.org/pest-and-pesticide-management/guidelines-standards/faowhojoint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/en/

FAO Specification 85/SG (December 2016*)

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 (85/2001). It should be applicable to relevant products of this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers. The evaluation report (85/2001), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of granules containing technical dicamba, complying with the requirements of the FAO specification 85/TC (November 2023), in the form of dicamba sodium salt, together with carriers and any other necessary formulants. It shall be homogeneous, free from visible extraneous matter and/or hard lumps, free flowing, and nearly dust free or essentially non-dusty. The active ingredient shall be soluble in water. Insoluble carriers and formulants shall not interfere with compliance with clause 3.2.

2 Active Ingredient

2.1 Identity tests (CIPAC 85/WG/M/2, Handbook K, p. 36, 2003) (Note 1)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 Dicamba content (CIPAC 85/WG/M/3, Handbook K, p. 36, 2003) (Note 1)

The dicamba content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the following tolerances:

Declared content in g/kg	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
Note: In each range the upper limit is included.	

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: https://www.fao.org/pest-and-pesticide-management/guidelines-standards/faowhojoint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/en/

3 Physical properties

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

pH range: 5 to 10

3.2 Degree of dissolution and solution stability (MT 179.1, CIPAC Handbook O, p. 189, 2017)

Residue of formulation retained on a 75 µm test sieve after dissolution in CIPAC standard water D at 25 ± 5°C (Note 2).

Maximum: 2 % after 5 min.
Maximum: 2 % after 24 h.

3.3 Persistent foam (MT 47.3, CIPAC Handbook O, p. 177, 2017)

Maximum 30 ml after 1 min.

3.4 Dustiness (MT 171.1, CIPAC Handbook P, p. 235, 2021) (Note 3)

The formulation shall have a maximum collected dust of 30 mg by the gravimetric method.

3.5 Flowability (MT172.2, CIPAC Handbook P, p. 241, 2021) (Note 4)

At least 99 % of the formulation shall pass through a 5 mm test sieve after 20 drops of the sieve.

4 Storage stability

4.1 Stability at elevated temperatures (MT 46.4, CIPAC Handbook P, p.232, 2021)

After storage at 54 ± 2 °C for 14 days the determined average active ingredient content shall not be lower than 95 % relative to the determined average content found before storage (Note 5) and the formulation shall continue to comply with the clauses for:
-pH range (3.1),
-degree of dissolution and solution stability (3.2),
-dustiness (3.4).

Note 1 The CIPAC method for confirmation of the identity and determination content of dicamba in granular formulations refers to water dispersible granules (WG). However, due to the high solubility of dicamba sodium salt the granular formulation is rather a soluble granule (SG) following the definitions for this type of formulation and the CIPAC method is considered to be applicable for SG as well.

Note 2 The mass of sample to be used in the test should be specified at the highest rate recommended by the supplier. The test is to be conducted in CIPAC standard water D.

Note 3 The optical method of MT 171.1 usually shows good correlation with the gravimetric method and can, therefore, be used as an alternative where the equipment is available. Where the correlation is in doubt, it must be checked with the formulation to be tested. In case of dispute the gravimetric method shall be used.

Note 4 The revised MT 172.2 superseeds MT 172.1.

Note 5 Samples of the formulation taken before and after the storage stability test may be analyzed together after the test in order to reduce the analytical error.

DICAMBA SOLUBLE CONCENTRATE

FAO Specification 85/SL (December 2016*)

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 (85/2001). It should be applicable to relevant products of this manufacturer but it is not an endorsement of those products, nor a guarantee that they comply with the specification. The specification may not be appropriate for the products of other manufacturers. The evaluation report (85/2001), as PART TWO, forms an integral part of this publication.

1 Description

The material shall consist of technical dicamba, complying with the requirements of FAO specification 85/TC (December 2023), in the form of dicamba dimethylammonium, potassium or sodium salt, 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 (CIPAC 85/SL/M/2, Handbook K, p. 35, 2003)

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 Dicamba content (CIPAC 85/SL/M/3, Handbook K, p. 35, 2003)

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

Declared content in g/kg	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
Note: In each range the upper limit is included.	

* Specifications may be revised and/or additional evaluations may be undertaken. Ensure the use of current versions by checking at: https://www.fao.org/pest-and-pesticide-management/guidelines-standards/faowhojoint-meeting-on-pesticide-specifications-jmps/pesticide-specifications/en/

3 Physical properties

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

pH range: 5 to 10

3.2 Dilution stability (MT 41.1, CIPAC Handbook O, p. 174, 2017) (Note 2)

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

3.3 Persistent foam (MT 47.3, CIPAC Handbook O, p. 177, 2017)

Maximum 30 ml after 1 min.

4 Storage stability

4.1 Stability at 0ºC (MT 39.3, CIPAC Handbook J, p.126, 2000)

After storage at 0 ± 2 °C for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

4.2 Stability at elevated temperatures (MT 46.4, CIPAC Handbook P, p.232, 2021)

After storage at 54 ± 2 °C for 14 days the determined average active ingredient content shall not be lower than 95 % relative to the determined average content found before storage (Note 3) and the formulation shall continue to comply with the clauses for:
-pH range (3.1),
-dilution stability (3.2).

Note 1 If the buyer requires both g/kg and g/L, then in case of dispute the analytical results shall be calculated as g/kg.

Note 2 The formulation should be tested at 1.0 % w/v.

Note 3 Samples of the formulation taken before and after the storage stability test may be analyzed together after the test in order to reduce the analytical error.

PART TWO

EVALUATION REPORTS

Recommendations

(i) the dicamba TC proposed by M/s Hemani Industries Ltd. should be accepted as equivalent to the dicamba reference profile.
(ii) the existing FAO specification for dicamba TC should be extended to encompass the technical material manufactured by M/s Hemani Industries Ltd.

Appraisal

The meeting considered data and supporting information submitted in 2023 by M/s Hemani Industries Ltd. for the determination of the equivalence with the existing FAO specification for dicamba.

The data submitted for the TC specification were in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for pesticides and supported the existing specification. [FAO/WHO Manual, 2022].

Dicamba was evaluated by the WHO IPCS in 2019 [IPCS, 2019] and by the FAO/WHO JMPR in 2010 (T, R), 2011 (R) and 2013 (R). [JMPR, 2010], [JMPR, 2013].

It was evaluated by U.S. EPA, the results were published in the Reregistration Eligibility Decision for dicamba (EPA 738R06905) [EPA, 2006]. Dicamba was evaluated by the European Commission as part of the EU review of existing active substances. [EFSA, 2011], [CIR, 2011].

The confidential data provided on the manufacturing process of dicamba are identical to those submitted for registration in Brasil. [Conf] The Meeting was provided with commercially confidential information on the manufacturing process and batch analysis data on all impurities present below or above 1 g/kg and their manufacturing limits in the TC. Mass balances were 99.12-99.25 % in the 5-batch data. The maximum limits for the impurities were supported by the 5-batch data and they were statistically justified.

The declared minimum active ingredient content (980 g/kg) was higher than that of the FAO specification. The Company confirmed that their product complies with the existing specification.

The manufacturing process, impurity profile and five batch analyses were compared with the data submitted by Gharda in 1999 (which was one of the reference proposers). The presented synthetic pathway of this technical material was identical with that of the reference technical material. The impurity profiles were different, Hemani Industries profile containing less impurities, with lower specification limits, however there were two new impurities, one not specified as its content in the 5-batches was below 1 g/kg. The impurity below 1 g/kg was considered not relevant at levels < 1 g/kg in dicamba technical based on toxicological considerations. The other new impurity was considered non-relevant based on a comparative (Q)SAR analysis (with DEREK) of dicamba and a structurally similar impurity. The maximum limits for the impurities were supported by the batch data.
Analyses of dicamba technical product demonstrated that dioxins and furans were below the LOQ values. The toxic equivalency (TEQ) results of the dicamba technical samples varied between 0.001 and 0.514 ng/kg (ppt).

The proposer used an in-house HPLC-UV method with external standardization for the determination of the active ingredient content in dicamba TC instead of the CIPAC official method published in CIPAC Handbook K. The company provided a bridging study to

compare the results of the in-house method with those obtained using the collaboratively validated CIPAC method. The results demonstrated that the results in the 5-batch study using the in-house method are similar with the results using the official CIPAC method.

The organic impurities were determined by HPLC with UV detection. Identity of the active ingredient dicamba in the technical batches was confirmed by IR, NMR and MS. Identity of all impurities was confirmed by IR, NMR and MS. Residual water was analyzed by Karl-Fischer titration. [CIPAC, F] Material insoluble in acetone was determined according to CIPAC MT 27 [CIPAC, F].

Test methods for determination of physico-chemical properties of the technical active ingredient were CIPAC, OECD and EC.

The total dioxins and furans were determined by high resolution gas chromatography/HRMS and the total content in the test substance was expressed as the impurity 2,3,7,8-TCDD (2,3,7,8-tetrachlorodibenzo-*p*-dioxin).

Data on physical-chemical properties, like melting point, boiling point, partition coefficient, vapour pressure, hydrolysis, water solubility and solubility in organic solvents, for technical material (97.86 %) were provided. Toxicity data were available for mutagenicity profile (Ames test, micronucleus test) derived from the technical grade active ingredient manufactured by the proposer with a purity of 97.86%. Results were similar to those provided for the reference profile. Data were available also for acute toxicity, irritation and sensitization.

Considering the absence of mutagenicity in the OECD 471 and OECD 474 tests, the Meeting concluded that the M/s Hemani Industries Ltd dicamba TC was equivalent to the dicamba reference TC based on Tier-1.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 85/2023

Table 1. Chemical composition and properties of dicamba technical material (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied and held on file by FAO and or WHO. Mass balances were [99.13 – 99.25] % and percentages of unknowns were [0.74-0.87] %.
Declared minimum dicamba content	980 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None
Relevant impurities < 1 g/kg and maximum limits for them:	None
Stabilisers or other additives and maximum limits for them:	None

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting range of the TC	114°C	97.86	OECD 102	G11192
Solubility in organic solvents	Solubility at 20°C methanol >250 g/L acetone 57-67 g/L 1,2- dichloroethane 50-57 g/L ethyl acetate 50-57 g/L *p*-xylene 50-57 g/L *n*-heptane 2.18 g/L	97.86	OECD 105 CIPAC MT 181	G11189

Formulations and co-formulated active ingredients

The main formulation types available are GR and SL (agricultural formulations).

Methods of analysis and testing

The analytical method for the active ingredient (including identity tests) is in-house validated HPLC method.
The method(s) for determination of impurities are based on in-house validated HPLC-DAD method. CIPAC Method MT 30.5 (Karl Fischer titration method) was used for determination of moisture content and CIPAC Method MT 27 for material insoluble in acetone.
Test methods for determination of physico-chemical properties of the technical active ingredient were OECD and CIPAC methods, as indicated in the specifications.

Expression of the active ingredient

The active ingredient is expressed as dicamba.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

(i) The proposer confirmed that the mutagenicity data included in the summary below were derived from dicamba 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 2. Mutagenicity profile of the technical material based on *in vitro* and *in vivo* tests

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Salmonella typhimurium [TA98, TA100, TA1537, TA1535] *E.Coli* -WP2uvrA (pKM101)	Reverse mutation (*in vitro*)	97.86	OECD 471 Doses: Trial I- 32, 101, 320, 1013, 3200, 5000 µg/plate in DMSO with and without metabolic activation Trial II- 100, 266, 707, 1880, 3066, 5000 µg/plate in DMSO with and without metabolic activation	Negative	G11209
Mice, Swiss Albino Male & Female	Micronucleus Test (*in vivo)*	97.86	OECD 474, Doses: 90, 190, 375 mg/kg (24h) in [0.5 % (w/v) Sodium carboxymethyl cellulose (medium viscosity) with 0.1 % (v/v) Tween 80 in Milli-Q water]	Negative	G11210

ANNEX 2

REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
FAO/WHO Manual, 2022		2022	https://www.fao.org/3/cb8401en/cb8401en.pdf
IPCS, 2019		2019	https://apps.who.int/iris/bitstream/handle/10665/332193/9789240005662-eng.pdf?sequence=1&isAllowed=y p.30 https://apps.who.int/iris/bitstream/handle/10665/342924/9789241655347-eng.pdf?sequence=1&isAllowed=y p.75
JMPR, 2010		2010	https://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Evaluation10/Dicamba.pdf
JMPR, 2013		2013	https://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Evaluation13/Dicamba.pdf https://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Report13/5.11_DICAMBA__240_.pdf
EPA, 2006		2006	https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P10049M3.txt
EFSA, 2011		2011	https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2011.1965
CIR, 2011		2011	https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32011R1100&qid=1683930085453
Conf		2023	e-mail confirming the similarity of data package submitted to Brasil and to JMPS. Date: 7.06.2023.
CIPAC, F	Martijn A and Dobrat W	1995	CIPAC Handbook Volume F. Physico-chemical Methods for Technical and Formulated Pesticides
G11192	H.S. Anand	2016 +	Determination of Melting Point of Dicamba technical. Study No. G11192. GLP. M/s Hemani Industries Ltd, India. Unpublished
G11189	H.S. Anand	2016	Determination of Solubility of Dicamba technical in Organic Solvents. Study No. G11189. GLP. M/s Hemani Industries Ltd, India. Unpublished
G11209	G. Joel Sathiyaseelan	2016	Dicamba Technical: Bacterial Reverse Mutation Test. Study No. G11209. GLP. M/s Hemani Industries Ltd, India. Unpublished.
G11210	H.N. Krishnamurthy	2017	Mammalian Erythrocyte Micronucleus Test following oral administration of Dicamba Technical to Swiss Albino Mice. Study No. G11210. GLP. M/s Hemani Industries Ltd, India. Unpublished.

Recommendations

(i) the dicamba TC proposed by Jiangsu Yangnong Chemical Co., Ltd. should be accepted as equivalent to the dicamba reference profile.
(ii) the existing FAO specification for dicamba TC should be extended to encompass the technical material manufactured by Youjia Crop Protection Co., Ltd. (a subsidiary company of Jiangsu Yangnong Chemical Co., Ltd.).

Appraisal

The meeting considered data and supporting information submitted in 2015 by Jiangsu Yangnong Chemical Co., Ltd. (Jiangsu Yangnong) for the determination of the equivalence of dicamba TC with the reference profile. The data submitted were in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for Pesticides (2nd revision of the 1st edition of the manual, 2010) and supported the existing specification. The reference specification and supporting data for dicamba were provided by Syngenta Crop Protection AG (formerly Novartis Crop Protection), BASF and Gharda Chemicals Limited in 1999 and FAO specifications had been published in 2001.

Dicamba is the ISO common name for 3,6-dichloro-2-methoxybenzoic acid according to IUPAC nomenclature. It is a synthetic auxin belonging to the benzoic acid herbicide family. It is a post-emergent herbicide for the control of annual and perennial broadleaved weeds in tolerant crops like corn.

Dicamba was evaluated by JMPR, with the most recent JMPR evaluation in 2010. JMPR established an acceptable daily intake (ADI) 0-0.3 mg/kg bw based on long term studies in rats and an acute reference dose (ARfD) of 0.5 mg/kg bw.

Dicamba is not under patent and the main formulation types available are SL and SG.

The Meeting was provided with commercially confidential information on the manufacturing process for dicamba, five-batch analysis data on all impurities present below or above 1g/kg and their manufacturing limits in the TC. Mass balances ranged from 98.6% to 98.76% in the 5-batch data. The maximum limits for the impurities were supported by the 5-batch data and they are statistically justified. The proposer declared the minimum purity of the dicamba TC as 980 g/kg which is statistically justified (mean value-3 standard deviation: 984.16 g/kg) and it is higher than the existing FAO specification. (not less than 850 g/kg). Confidential data were similar to those submitted for registration in China (Conf).

The manufacturing process, impurity profile and five batch analyses were compared with the data submitted by the reference proposers. There are differences in the solvents being used and there is different number of steps in each process. However, the starting materials are the same in both cases. The impurity profile of Jiangsu Yangnong is different as it has fewer impurities than the reference profile. In Jiangsu Yangnong five batch analysis data three impurities were present. Two of them are the same with those detected in the reference profile with lower manufacturing specification limits. The other one is a residual solvent (new compound) used in the final synthesis step. This solvent was not used in the manufacturing process of the reference profile and for that reason was not detected. In the case of Jiangsu Yangnong's TC this solvent was found at low level (≤ 0.28 g/kg) in the five batch analysis, however it was included in the specifications of Jiangsu with a limit of 0.5 g/kg. The Meeting requested the manufacturer to justify this specification and whether this impurity should be considered as relevant. The proposer explained that the analysis of the remaining solvent

had been requested for EU registration and for that reason was included in the five batch analysis data and confirmed that the remaining solvent at the concentration level found (0.5 g/kg) was not considered as relevant. The Meeting considered that the WHO air quality guideline for the remaining solvent is not exceeded for worker exposure to dicamba and confirmed that this is not considered as relevant impurity.

An *in-vitro* mutagenicity test on Jiangsu Yangong's dicamba had been conducted as Tier-1 data. The results of the study allowed the conclusion that the test material did not induce reverse mutation in the *E. coli* strains used in the assay with and without metabolic activation.

In addition, the company submitted a study that polychlorinated dibenzodioxins and polychlorinated dibenzofurans in their technical material are not present at or above the level of 0.01 ng/g [acceptable 2,3,7,8-tetrachlordibenzo-*p*-dioxin (TCDD) toxic equivalents (TEQ): max 10 ppb or 0.01 ng/g]. The analysis performed by GC/HRMS (high resolution mass spectrometry). The method presented was validated with regard to specificity, linearity of response, linearity range, limits of detection and quantification, precision and accuracy in an external laboratory (Study No RF. 14897.030.004.14).

The proposer used a validated in-house HPLC-UV method with external standardization for the determination of the active ingredient content of dicamba in dicamba TC instead of the CIPAC official method published in CIPAC Handbook K. The in-house method was validated for its specificity, linearity of response, linearity range, limits of detection and quantification, precision and accuracy in an external laboratory. At the request of the Meeting, the proposer provided a bridging study where the same batches were analysed using the CIPAC method for that compound. The analysis results showed that the two methods gave comparable results and the results in the 5-batch analysis study based on the in-house method were considered valid by the meeting. Two different methods were used for the determination of the detected impurities. For one impurity (the remaining solvent) a validated GC/MS method had been used, whereas for the determination of the other impurity an external standardization HPLC-UV method had been used. Both methods are validated with respect to specificity, linearity of response, precision, accuracy, limit of detection and quantification.

Test methods for determination of physico-chemical properties of the technical active ingredient were OECD.

The confirmation of the identity of dicamba was done using a comparison ^{1}H-NMR spectra of the TC and a reference material.

The Meeting was provided with data on melting point and solubility in water and organic solvents. The difference in melting point range is due to the difference in purity of the test materials (99.2 % versus 98.66 % in the reference TC).

The data submitted allowed the Meeting to conclude on equivalence of Jiangsu Yangnong technical dicamba with the reference profile. The Meeting concluded that Jiangsu's dicamba TC was equivalent to the dicamba reference TC based on Tier-1 evaluation as detailed in the Manual.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 85/2016

Table 1. Chemical composition and properties of dicamba technical materials (TC)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data		Confidential information supplied and held on file by FAO. Mass balances were 98.60 – 98.76% and percentages of unknowns ranged from 1.24-1.40 %.		
Declared minimum dicamba content		980 g/kg		
Relevant impurities ≥ 1 g/kg and maximum limits for them		None		
Relevant impurities < 1 g/kg and maximum limits for them:		None		
Stabilisers or other additives and maximum limits for them:		None		
Parameter	Value and conditions	Purity %	Method reference	Study number
Melting range of the TC	115.0-115.7°C	98.66	OECD 102	14897.005.011.14
Solubility in organic solvents	990.22 g/L in acetone and 825.06 g/L in methanol at 20.1°C.	98.66	OECD 105	14897.008.015.14

FORMULATIONS AND CO-FORMULATED ACTIVE INGREDIENTS

The main formulation types available are SG and SL. In these formulations, dicamba is present in the form of a salt (e.g sodium or dimethylamine salt).

METHODS OF ANALYSIS AND TESTING

The CIPAC method for the determination of dicamba content in dicamba TC is based on a reversed-phase HPLC on a C18-column with UV detection at 280 nm and external standardization. The method is published in CIPAC Handbook K and also includes identity tests for dicamba based on comparison of HPLC retention time and infrared spectra.
The in-house method proposed by Jiangsu Yangnong for the determination of dicamba content was successfully compared with the CIPAC method 85/TC/M in a bridging study. The in-house method is based on reversed phase HPLC with an Eclipse XDB-C18 column, using UV detection at 230 nm and external standardization.
Three different methods were submitted for the determination of the three detected impurities. The method for the determination of impurity A is a reversed phase HPLC method whereas the method used for the determination of the remaining solvent is a validated GC-MS method. Finally a Karl Fischer titration method was submitted for the determination of the third impurity.
Test methods for determination of physico-chemical properties of the technical active ingredient were OECD as indicated in the specifications.

EXPRESSION OF THE ACTIVE INGREDIENT

The active ingredient is expressed as dicamba (free acid).

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

(i) The proposer confirmed that the mutagenicity data included in the summary below were derived from dicamba 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 2 Mutagenicity profile of the technical material based on *in-vitro* tests

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Salmonella typhimurium test strains: TA97a, TA98, TA100, TA102 and TA1535	Ames test	98.05	OECD 471 0.03, 0.1, 0.3, 1.0, 3.0 and 5.0 mg/plate (in both the presence and absence of S9 mix) 37^{o}C for 48 hours	Not mutagenic	14897.401.058.15

Jiangsu Yangnong provided data on *in vitro* mutagenicity of dicamba technical material. The results of the study allow the conclusion that dicamba TC produced by the company does not lead to reverse mutations in the strains included in the test.

According to the harmonized classification and labelling (CLP Regulation), the classification for dicamba is: Acute Toxicity (Category 4): hazard statement H302, aquatic chronic (category 3): hazard statement H412 and eye damage (category 1): hazard statement-H318.

ANNEX 2

REFERENCES

(sorted by study number)

Study number	Author(s)	year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
	FAO	2001	FAO specification: 85/TC and evaluation report 85/2001, accessible at http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/jmps/en/.
Conf		2015	e-mail from ICAMA, confirming the similarity of confidential data submitted to China and JMPS
14897.030.004.14		2015	Qualitative and Quantitative Profile of the test substance DICAMBA TC (Five Batch Analysis). 14897.030.004.14. RF.14897.030.004.14. GLP.
14897.005.011.14		2015	Melting point and range of DICAMBA TC. 14897. 005.011.14. RF. 14897. 005.011.14. GLP.
14897.008.015.14		2015	Solubility in water and organic solvents of DICAMBA TC. 14897.008.015.14. RF. 14897.008.015.14. GLP.
14897.401.058.15		2015	Evaluation of the mutagenic potential of the test substance Dicamba TC by reverse mutation assay in Salmonella enteric serovar Typhimurium (Ames Test). 14897.401.058.15. RF. 14897.401.058.15. GLP.

DICAMBA

EVALUATION REPORT 85/2001

Explanation

The data for dicamba were evaluated in support of review of existing FAO specifications AGP:CP/59, 1975.

Dicamba is not under patent.

Dicamba has not been evaluated by the FAO/WHO JMPR and WHO/IPCS. It is to be reviewed by the European Commission as a "list 3" compound (2003 onwards); it is not under review by the US EPA.

The draft specification and the supporting data were provided by Syngenta Crop Protection AG (initially by Novartis Crop Protection), BASF and Gharda Chemicals Ltd. in 1999.

Uses

Dicamba is a selective systemic herbicide, absorbed by the leaves and the roots, with ready translocation throughout the plant via both the symplastic and apoplastic systems. It is used in agriculture (cereals, maize, sorghum, sugar cane, asparagus, perennial seed grasses, turf, pastures, rangeland and non crop land) against annual and perennial broad-leaved weeds and brush species (Pesticide Manual).

Identity of the active ingredient

ISO common name

Dicamba (E-ISO, (m) F-ISO)

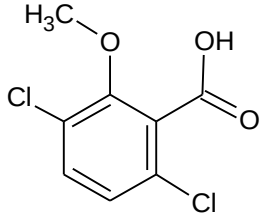
Chemical name(s)

IUPAC: 3,6-dichloro-*o*-anisic acid)
CA: 3,6-dichloro-2-methoxybenzoic acid

Synonyms

Dicamba (BSI, ANSI, WSSA), MDBA (JMAF)

Structural formula



Molecular formula

$C_8H_6Cl_2O_3$

Relative molecular mass

221.0

266.1 (dimethylammonium salt)

259.1 (potassium salt)

243.0 (sodium salt)

CAS Registry number

1918-00-9

CIPAC number

85

Identity tests

IR spectrum,HPLC retention time

Physico-chemical properties of pure dicamba (Table 1)

Parameter	Value(s) and conditions	Purity %	Method reference
Vapour pressure	1.67×10^{-3} Pa at 25 °C (extrapolated)	99.2	OECD 104 EEC A4
Melting point, boiling point and/or temperature of decomposition	Melting point: 114 - 116°C Boiling point: 230°C Decomposition temperature: 230°C	99.2 99.6	OECD 102 OECD 103
Solubility in water	6.6 g/l at 25°C at pH 1.8 >250 g/l at pH 4.1 >250 g/l at pH 6.8 >250 g/l at pH 8.2	99.6	OECD 105
Octanol/water partition coefficient	log P_{OW} = -0.55 at 25°C at pH 5.0 log P_{OW} = -1.8 at 25°C at pH 6.8 log P_{OW} = -1.9 at 25°C at pH 8.9	99.6	OECD 107
Hydrolysis characteristics	No, or only very slight, degradation was observed at pH 5, 7 and 9 during 30 days at 25°C.		OECD 111 EPA 540/9-82-021
Photolysis characteristics	aqueous photolysis: DT_{50} = 14-50 d (latitude: Cincinnati, Ohio)		EPA N,161-2
Dissociation characteristics	pKa = 1.87	99.6	OECD 112

Chemical composition and properties of dicamba technical material (TC) (Table 2)

Manufacturing process, maximum limits for impurities ≥ 1 g/kg, 5 batch analysis data	Confidential information supplied by both manufacturers and held on file by FAO. Mass balances were 96.36 to 100.86% and percentages of unknowns were 0.0 to 3.6%.
Declared minimum dicamba content	850 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	None.
Relevant impurities < 1 g/kg and maximum limits for them:	None.
Stabilisers or other additives and maximum limits for them:	None.
Melting or boiling temperature range of the TC and/or TK	melting point 87– 108°C

Toxicological summaries

Notes.

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

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

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

Species	Test	Duration and conditions or guideline adopted	Result
Rat male Rat female	oral	acute	LD_{50} = 1879 mg/kg bw LD_{50} = 1581 mg/kg bw
Rabbit	dermal	24 h	LD_{50} > 2000 mg/kg bw
Rat (dust)	inhalation	4 h	LC_{50} = 6900 mg/m^3
New Zealand White rabbits	skin irritation	4 h	Not irritant
New Zealand White rabbits	eye irritation	24 h	Due to its acidic nature, dicamba is strongly irritant to the eye
Guinea pigs	skin sensitization	acute	Dicamba is not sensitising in the maximisation test (Magnusson and Kligman)

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

Species	Test	Duration and conditions or guideline adopted	Result
Rats, Beagle dog	oral (sub-acute/sub-chronic toxicity)	rat: 90 d dog: 1 y	NOAEL = 239 to 342 mg/kg bw/d (rat), 52 mg/kg bw/d (dog) LOEL = 682 to 1000 mg/kg bw/d (rat)
Rat, Mouse	feeding, carcinogenicity	lifetime	in the combined chronic toxicity/carcinogenicity study, no carcinogenic potential was found up to highest tested dose of 3000 ppm.
Rat	feeding, multi-generation and reproduction	OECD 416	NOAL = 35 to 105 mg/kg bw/d LOEL = 105 to 347 mg/kg bw/d
Rabbit	teratogenicity and developmental toxicity	20 d	no developmental toxicity or teratogenicity observed
Rat	delayed neurotoxicity		no potential expected from acute and sub-chronic studies

Mutagenicity profile of dicamba technical material based on *in-vitro* and *in-vivo* tests

The mutagenic potential of dicamba has been studied in various *in-vitro* and *in-vivo* test systems (Ames test, CHO cells, micronucleus). Based on these results, dicamba is not considered to be a mutagen.

Table 5. Ecotoxicology profile of dicamba technical material

Species	Test	Duration and conditions	Result
Daphnia magna (water flea)	acute toxicity	24 and 48 h (static exposure)	EC_{50} = 110.7 mg/l
Rainbow trout Bluegill sunfish Sheepshead minnow	acute toxicity	96 h (static exposure)	LC_{50} = 135 mg/l LC_{50} = 135 mg/l LC_{50} > 180 mg/l
Scenedesmus subspicatus alga	acute	96 h	EC_{50} = 269 mg/l NOEC = 250 mg/l
Apis *mellifera* (honey bee)	acute oral, acute contact	72 h	LD_{50} =>0.1 mg/bee
Bobwhite quail, Mallard duck	acute toxicity	acute	LD_{50} = 216 – 2009 mg/kg bw
Mallard duck	short-term toxicity	5 d	LC_{50} > 10.000 mg/kg diet

Dicamba has not been evaluated by the WHO/PCS or the FAO/WHO JMPR. The WHO/PCS hazard classification of dicamba is Class III, slightly hazardous.

Formulations and co-formulated active ingredients

The main formulation types available are SG and SL. In these formulations, dicamba is present in the form of a salt.

Dicamba may be co-formulated with a wide variety of other herbicides, such as 2,4-D or other phenoxy acids, sulfonylureas or triazines.

These formulations are registered and sold in many countries: Argentina, Australia, Belarus, Belgium, Bolivia, Brazil, Bulgaria, Canada, Chile, China, Czech Republic, Denmark, Dominican Republic, Estonia, France, Germany, Greece, Hungary, India, Indonesia, Italy, Iraq, Kazakhstan, Kenya, Korea, Latvia, Lithuania, Malaysia, Mexico, Moldavia, Netherlands, Norway, Panama, Saudi Arabia, Slovak Republic, South Africa, Spain, Serbia, Switzerland, Tanzania, Thailand, Trinidad, Tobago, Turkey, Ukraine, United Kingdom, USA, Uruguay, Uzbekistan, Zimbabwe.

Methods of analysis and testing

The analytical methods for the active ingredient (including identity tests) are CIPAC method 85.102/SL/M/2 or 3 (CIPAC Handbook H, p.128) or the more recent full CIPAC method m/4177 (not yet published but available from FAO Plant Production and Protection Division or the CIPAC secretariat). Dicamba is determined by IR spectroscopy in the earlier method or by reversed-phase HPLC, using UV detection at 280 nm and external standardisation, in the later method. An alternative HPLC method has been validated by Gharda Chemicals according to OECD and US EPA Guidelines for Good Laboratory Practice (GLP).

The analytical methods for determination of (non-relevant) impurities were based on reversed phase HPLC using UV detection at 280 nm and external standardisation.

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

Physical properties

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

Containers and packaging

No special requirements for containers and packaging have been defined but containers should comply with pertinent national and international transport and safety regulations.

Expression of the active ingredient

The active ingredient is expressed as dicamba (free acid).

Appraisal

The data for dicamba were evaluated in support of review of an existing FAO specification (AGP:CP/59 – 1975). Dicamba is not under patent.

Dicamba is a selective systemic herbicide, used in agriculture, mainly for the control of broadleaved weeds in various monocotyledonous crops. It is not patented and is registered in many countries throughout the world.

Dicamba, in the form of its salts, is highly water soluble and it is formulated (and co-formulated) as soluble concentrates (SL) or soluble granules (SG). In these formulations, dicamba is present as the dimethylamine, sodium or potassium salt but it is determined analytically as dicamba free acid and the content of active ingredient is expressed as the free acid. The proposers initially considered the SG to be a water dispersible granule (WG), and the CIPAC HPLC method was recorded as having been validated for the WG. However, the salt of the active ingredient is fully soluble in water and the “WG” is clearly an SG.

Dicamba is classified as slightly hazardous on the basis of its acute toxicity but, because it is a rather strong acid (pKa 1.9), the free acid is irritating to the eye.

Each of the proposers provided the meeting with confidential information on their manufacturing process and 5 batch analysis data on the technical materials, including all impurities present at > 1 g/kg and some at lower levels. The data submitted were in accordance with the requirements of the FAO Manual (5th edition) and supported the draft specifications.

The IR analytical method and the HPLC analytical method for the determination of the active ingredient in technical and formulated products have been collaboratively tested by CIPAC. The IR method has been published, the HPLC method is not yet published but has been accepted as full CIPAC method. In addition, there is a validated HPLC method from Gharda (method available from the Pesticide Information Officer, FAO Plant Production and Protection Division).

The meeting agreed that the reference profile of purity and impurities should be that of BASF and Syngenta, with a minimum purity of 850 g/kg, because it was supported by the most complete data on toxicology and ecotoxicology. No impurities were considered to be relevant. The meeting agreed that the technical material manufactured by Gharda was equivalent to that of BASF and Syngenta.

Recommendations

The meeting recommended that the specifications for TC, SL and SG should be adopted by FAO and that the reference profile (for the determination of equivalence) should be that submitted by BASF and Syngenta.

References

FAO Manual	Manual on Development and Use of FAO specifications for Plant Protection Products, 5th edition, January 1999, Rome.
CIPAC Handbook H.	Dobrat W and Martijn A (ed), Black Bear Press, Cambridge. 359 p.,1998.
WHO/PCS	The WHO recommended classification of pesticides by hazard and guidelines to classification 1998-1999, WHO/PCS/98.21/rev1, 1998.
Pesticide Manual	Tomlin C.D.S. (ed), The Pesticide Manual, 11th edition. British Crop Protection Council, 1997.
CIPAC Handbook F	Dobrat W and Martijn A (ed), Black Bear Press, Cambridge. 472 p., 1995.