Food and Agriculture Organization
of the United Nations

FAO SPECIFICATIONS AND EVALUATIONS FOR AGRICULTURAL PESTICIDES

2.4-D

(2,4-dichlorophenoxy)acetic acid

2023

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DISCLAIMER[1]

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

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

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

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

INTRODUCTION

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

From 1999 onward, the development of FAO specifications follows the **New Procedure**, described first in the 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

2.4-D

2,4-D

INFORMATION

ISO common name

2,4-D (ISO 1750 (published))

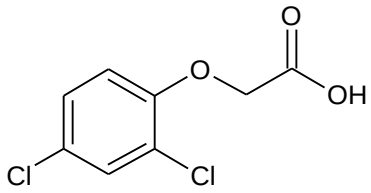
Chemical name(s)

IUPAC: (2,4-dichlorophenoxy)acetic acid
CA: 2-(2,4-dichlorophenoxy)acetic acid

Synonyms

2,4-D acid

Structural formula



Molecular formula

$C_8H_6Cl_2O_3$

Molar mass

221.0 g/mol

CAS Registry number

94-75-7

CIPAC number

1

Identity tests

IR/FTIR (CIPAC MT 1/TC/M3/2.2), HPLC (CIPAC MT 1/TC/M3/2.5) retention time, LC-MS, NMR

FAO Specification 1/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 (1/2020 & 1/2023). 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 (85/2020 & 1/2023), as PART TWO, form an integral part of this publication.

1 Description

The material shall consist of 2,4-D together with related manufacturing impurities, in the form of white to brown crystals, granules, flakes, powder or lumps with faint phenolic odour, and shall be free from visible extraneous matter and added modifying agents.

2 Active Ingredient

2.1 Identity tests (1/TC/M3/2, CIPAC 1C, p. 2060)

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 2,4-D content (1/TC/M3/5.2, CIPAC 1C, p.2062)

The 2,4-D content shall be declared (not less than 960 g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

3 Relevant impurities (Notes 1 & 2)

3.1 Free phenols (MT 69.1, CIPAC F, p.197; MT 155.1, CIPAC F, p. 362) (Note 3)

Maximum: 3 g/kg, calculated as 2,4-dichlorophenol.

Note 1 In addition to the relevant impurities to be controlled in products of the manufacturers identified in evaluation report 1/2020, residues of 2-chlorophenoxy acetic acid and 4-chlorophenoxy acetic acid may occur at low levels. In case these levels would exceed ≥ 9 g/kg and ≥ 6 g/kg respectively in the products of other manufacturers, they may be designated as relevant impurities and clauses may be required to limit their concentrations.

Note 2 In addition to the relevant impurities to be controlled in products of the manufacturers identified in this evaluation report, polychlorinated dioxins and furans may occur as a result of certain manufacturing processes. If the content of these compounds expressed as 2,3,7,8-tetrachlorodibenzodioxin (2,3,7,8-TCDD) toxic equivalents (TEQ) exceeds 10.0 µg/kg (of 2,4-D) in the products of other manufacturers, they are designated as relevant impurities and a clause may be required to limit their concentration. The WHO model for calculation of the TEQ is used (van den Berg M. et al., Toxicol. Sciences 93(2), 223–241 (2006)).

Note 3 When using method MT 155.1, 2,4-dichlorophenol standard should be used.

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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/

PART TWO

EVALUATION REPORTS

Recommendations

(i) the 2.4-D TC proposed by M/s Hemani Industries Ltd. should be accepted as equivalent to the 2.4-D reference profile.
(ii) the existing FAO specification for 2.4-D 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 2.4-D. The FAO full specifications for 2,4-D were published in 2020 [FAO, 2020]

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].

2,4-D was evaluated by the WHO IPCS in 1984 and 1987 and by the FAO/WHO JMPR in 2001 and 2017.

The proposed specification for TC was essentially in accordance with the requirements of the FAO/WHO Manual.

The confidential data provided on the manufacturing process of 2,4-D were identical to those submitted for registration in Brasil. [Conf] The Meeting was provided with commercially confidential information on the manufacturing processes and batch analysis data on all impurities present below or above 1 g/kg and their manufacturing limits in the TC. Mass balances were 100.0-100.35 % in the 5-batch data.

The declared minimum active ingredient content (970 g/kg) was higher than that of the FAO specification.

The presented synthetic pathway of this technical material was identical with that of the products with the reference profile. The impurity profiles are different, Hemani Industries profile containing less impurities, with lower specification limits except for one non-relevant impurity where the specification was higher than the limit allowing a tier-1 equivalence, however based on the previous considerations of the evaluation report 1/2020, this impurity was also considered not relevant at the specified level. The maximum limits for the impurities were supported by the batch data.

The formation of tetra- to octa-chlorinated dioxins and furans is theoretically possible. Dioxins and furans can occur as a result of certain manufacturing processes. Analyses of 2,4-D technical product demonstrated that dioxins and furans were below the LOD values except for 2,3,7,8-TCDF. Concentrations of 2,3,7,8-TCDF were higher than LOD value but below the LOQ. The toxic equivalency (TEQ) results of the 2,4-D technical samples varied between 0.34 and 1.57 µg/kg (ppb).

The analytical method for the determination of the active ingredient in 2,4-D technical was HPLC with UV detection, similar to the existing CIPAC method. [CIPAC, 1C] The organic impurities were determined by HPLC with UV detection. Identity of the active ingredient 2,4-D

in the technical batches was confirmed by IR and NMR. Identity of all impurities was confirmed by IR, NMR and MS. Residual water was analyzed by Karl-Fischer titration. Sulphated ash was determined according to CIPAC MT 29. Material insoluble in triethanolamine was determined according to CIPAC MT 76.1, which is a method no longer supported by CIPAC.

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 were provided for technical material (97.5 %) on physical-chemical properties, like melting point, boiling point, partition coefficient, vapour pressure, hydrolysis, water solubility and solubility in organic solvents. 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 97.79%. Results were similar to those provided for the reference profile. Data were available also for acute toxicity, irritation and sensitization, not considered by the Meeting.

Considering the absence of mutagenicity in the OECD 471 and OECD 474 tests, the Meeting concluded that the M/s Hemani Industries Ltd 2,4-D TC was equivalent to the 2,4-D reference profile held on file by FAO based on Tier-1.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 1/2023

Table 1. Chemical composition and properties of 2.4-D 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 100.04-100.45 % and percentages of unknowns were 0 %.
Declared minimum 2,4-D content	970 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	Free phenols: maximum: 1.4 g/kg
Relevant impurities **<** 1 g/kg and maximum limits for them:	None
Stabilisers or other additives and maximum limits for them:	None

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC and/or TK	139.1 °C	97.79	OECD 102	G16677

Formulations and co-formulated active ingredients

The main formulation types available are EC, GR, SL, SP and WP (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-VWD/DAD method. CIPAC Method MT 30.6 (Karl Fischer titration method) was used for determination of moisture content, CIPAC Method MT 76 for triethanolamine insoluble, CIPAC Method MT 69.1 for free phenols (as 2,4-dichlorophenol) and CIPAC Method MT 29.1 for sulphated ash.

17 polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) was determined in 5 batches of 2,4-D technical grade active ingredient samples with validated EPA 821-B-94-005 method, “Method 1613: Tetra - Through Octa-Chlorinated Dioxins and Furans by Isotope Dilution HRGC/HRMS,” Revision B, October, 1994. [EPA 821-B-94-005]

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 2,4-D is expressed as 2,4-dichlorophenoxyacetic acid in g/kg or %w/w.

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

(i) The proposer confirmed that the mutagenicity data included in the summary below were derived from 2.4-D 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, TA 1535, TA1537, *E.Coli* -WP2uvrA (pKM101)]	Reverse mutation (*in vitro*)	97.79	OECD 471, Doses: Trial I and Trial II - 10, 32, 101, 320, 1012, 3200 µg/plate in DMSO with and without metabolic activation	Negative	G16693
Mice, Swiss Albino Male & Female	Micronucleus test (*in vivo)*	97.79	OECD 474, Doses: 35, 70, 140 mg/kg (24h) in [0.5 % (w/v) Sodium carboxymethyl cellulose (medium viscosity) in Milli-Q water and 0.1 % (v/v) Tween 80]	Negative	G16694

ANNEX 2

REFERENCES

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
FAO, 2020		2020	https://www.fao.org/3/cb0999en/cb0999en.pdf
FAO/WHO Manual, 2022		2022	https://www.fao.org/3/cb8401en/cb8401en.pdf
Conf		2023	e-mail confirming the similarity of data package submitted to Brasil and to JMPS. Date: 7.06.2023.
CIPAC, 1C	Henriet J, Martijn A and Povlsen H.H	1985	CIPAC Handbook Volume 1C. Analysis of Technical and Formulated Pesticides
EPA 821-B-94-005		1994	https://nepis.epa.gov/Exe/ZyPDF.cgi/9100E9BU.PDF?Dockey=9100E9BU.PDF
G16677	Swarnalatha J.	2021	Melting Point of 2,4-dichlorophenoxyacetic acid technical. Study No. G16677. GLP. M/s Hemani Industries Ltd, India. Unpublished.
G16693	S. Deepika Rani	2021	2,4-dichlorophenoxyacetic acid Technical: Bacterial Reverse Mutation Test. Study No. G16693. GLP. M/s Hemani Industries Ltd, India. Unpublished.
G16694	M. Latha	2021	2,4-dichlorophenoxyacetic acid Technical: Mammalian Erythrocyte Micronucleus Test following oral administration of to Swiss Albino Mice. Study No. G16694. GLP. M/s Hemani Industries Ltd, India. Unpublished.

Recommendations

The Meeting recommended that:

(i) the specification for 2,4-D TC, converted from the old procedure specification and proposed by the Industry Task Force II on 2,4-D Research Data, the EU 2,4-D Annex III Task Force and CAC Group Limited and as amended, should be adopted by FAO.

(ii) the FAO Specifications for 2,4-TC acid and variants, developed under the old procedure, should be withdrawn.

Appraisal

The FAO provisional specification for 2,4-D (1/TC/(S)/-) was published in 1984 [AGP:CP/100]. The FAO (full) specifications for the technical material (1/TC/S/F (1992)), sodium salts (1.1Na/TC/S/F (1992)) and esters (1.3/TC/S/F (1992)) were published in 1994 [AGP:CP/310].The compound was qualified as a candidate for conversion of „old procedure" into „new procedure" specification[1]. 2,4-D is not under patent.

The compound was evaluated by the WHO IPCS in 1984 and 1987 [IPCS, 1984], [IPCS, 1987]. and by the FAO/WHO JMPR in 2001 and 2017. [JMPR, 2001], [JMPR, 2017].

The Meeting evaluated data for 2,4-D in support of the conversion of the old procedure FAO specifications based on the draft specification and the supporting data provided by the Industry Task Force II on 2,4-D Research Data (membership is made up of Corteva Agriscience, Nufarm Americas, Inc. and Agro-Gor Corp., a U.S. corporation jointly owned by Albaugh, LLC and PBI-Gordon Corp., including the interests of two follow-on U.S. technical registrants: Tacoma Ag, LLC and Drexel Chemical Company.), the EU 2,4-D Annex III Task Force (membership is made up of Corteva Agriscience., Nufarm Europe Gmbh and ADAMA Manufacturing Poland S.A.) and CAC Group Limited in October 2018. Later on, CAC Group Limited announced[2] that the name of the company had changed to Jiangxi Tianyu Chemical Co., Ltd. This name change has been noted by FAO.

The data submitted were broadly in accordance with the requirements of the Manual on development and use of FAO and WHO specifications for pesticides (3rd revision of the first edition) and supported the proposed specification. [FAO/WHO Manual]

2,4-D is currently registered and sold in many countries throughout the world.

Statements were provided by Australian Pesticides and Veterinary Medicines Authority, Ministry of Agricultural Development & Food of Greece, Department of Plant Protection and Breeding of the Ministry of Agriculture and Rural Development of Poland and U.S. Environmental Protection Agency confirming that the confidential data on the manufacturing process and declaration of composition submitted to the FAO were the same as those submitted to the national regulatory authorities. [Conf1], [Conf2], [Conf3], [Conf4], [Conf5]

[1] see http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Specs/Call_for_data.pdf (September 2020)

[2] e-mail from Mrs. Huang dated August 31st 2020, formerly CAC Group Limited, to FAO with a formal request for a name change to now Jiangxi Tianyu Chemical Co., Ltd. effective immediately.

2,4-D is a white crystalline powder. It has a rather low volatility and has a melting point of 138.68°C. 2,4-D is moderately soluble in unbuffered water, however solubility increases up to 26.5 g/l in pH 10 buffered water. It is readily soluble in a number of organic solvents. The log Pow at pH 7 is -0.82. 2,4-D has a pK_a of 3.4.

The Meeting was provided with commercially confidential information on the manufacturing processes and batch analysis data on all impurities present below or above 1 g/kg and their manufacturing limits in the TCs. Mass balances were 99.8-100.2% in the 5-batch data.

The Meeting discussed whether or not there are more reference sources of 2,4-D or if a common reference specification should or could be defined and the individual specifications should be considered equivalent on the basis of the toxicological data on their impurities. All sources have similar manufacturing processes leading to different minimum content of the active ingredient, with no significant differences, and different impurity profiles. The Meeting considered that one specification should be developed covering all sources. The minimum active substance content of the technical materials is 960 g/kg, based on batch data from all the manufacturers.

The proposers suggested in their submissions that the same relevant impurities as in the old FAO specifications should be deemed relevant in the converted specification as well: free phenols, water, sulphated ash and triethanolamine insoluble.

The Meeting re-considered the relevance of these impurities and concluded that only free phenols should be deemed as relevant. Free phenols, consisting of 2,4-dichlorophenol, 2,6-dichlorophenol, 2,4,6-trichlorophenol and 4-chlorophenol, are expressed as 2,4-dichlorophenol. In the products of the manufacturers identified in this evaluation report 2,4,6-trichlorophenol, 2,6-dichlorophenol and 4-chlorophenol were found below LOQ (0.5 g/kg). 2-chlorophenoxy acetic acid (2-CPA) was proposed as skin irritant category 2 (GHS, but not harmonized classification), an adverse effect not caused by 2,4-D. Thus, 2-CPA was considered as a potentially relevant impurity. The acceptable concentration limit for the potential relevant impurity 2-CPA, based on the geometric mean of published LD_{50} values of 2,4-D (699, 443 and 486 mg/kg bw) [JMPR, 1996], [CIR, 2015] of 532 mg/kg bw. According to appendix H of the JMPS manual, the maximum acceptable concentration for 2-CPA is – based on the LD_{50} for 2-CPA and the geometric mean of the 2,4-D LD_{50} – 81.6 g/kg. The threshold limit for designating the impurity relevant is 8.16 g/kg. Rounding the limits to 90 g/kg and 9 g/kg, respectively, could be justified based on the different routes of administration –oral vs. peritoneal – and thus the possible overestimation of 2-CPA's toxicity relative to 2,4-D.

According to the JMPS Manual, the maximum concentration limits for skin irritants is 10 g/kg. Taking into account the values of all batches, where 2-CPA was found, it was proposed to consider this impurity as not relevant for the materials of the present evaluation.

4-chlorophenoxy acetic acid (4-CPA) was considered as a potentially relevant impurity based on the RfD of 2,4-D and 4-CPA and according to the JMPS manual, the maximum acceptable concentration for 4-CPA is 60 g/kg, at concentrations > 6 g/kg 4-CPA has to be considered a relevant impurity. Taking into account all batches, where 4-CPA was found, it was proposed to consider this impurity as not relevant for the materials of the present evaluation.

The formation of tetra- to octa-chlorinated dioxins and furans as byproducts in the manufacturing process cannot *a priori* be discounted. These dioxins and furans can be produced in trace amounts in certain manufacturing processes. Analyses of 2,4-D technical products demonstrate that dioxins and furans are rarely detected, and if detected, occur at extremely low levels in the technical materials subject of this evaluation. All members of the submission comply with the EU limit of dioxins and furans of TCDD toxic equivalents (TEQ) of

max 10 µg/kg (ppb). The Meeting considered dioxins and furans as relevant impurities in 2,4-D, if formed, and concluded to include a footnote in the specification. If the content of 2,3,7,8-tetrachlorodibenzodioxin (2,3,7,8-TCDD) toxic equivalents occurs at ≥ 10.0 µg/kg (of 2,4-D) [ToxSci] in the products of other manufacturers, it may be designated as a relevant impurity and a clause may be required to limit its concentration.

The active ingredient and impurities were quantified using validated high performance liquid chromatography with UV detection. Identity of the active ingredient 2,4-D in the technical batches was confirmed by IR and MS/MS. Identity of all impurities was confirmed by LC-MS/MS. Residual water was analyzed by Karl-Fischer titration. [CIPAC, F] Sulphated ash was determined according to CIPAC MT 29. [CIPAC, J] Material insoluble in triethanolamine was determined according to CIPAC MT 76.1, which is a method no longer supported by CIPAC. [CIPAC, F]

Five newer representative batches of technical 2,4-D were analysed for all notifiers for content of pure active substance, at the same laboratory, using the existing AOAC/CIPAC method of analysis for 2,4-D, to demonstrate that the current method was still satisfactory in analysing the 2,4-D content of all Task Force members' technical material. [CIPAC 1C]

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).

The proposed specification for TC was essentially in accordance with the requirements of the FAO/WHO Manual, however it was proposed to update the description concerning the odour and to remove water, sulphated ash and triethanolamine insoluble from the list of relevant impurities. It was agreed to add a note concerning the possible content of the relevant impurities dioxins and furans, 2-chlorophenoxy acetic acid and 4-chlorophenoxy acetic acid.

SUPPORTING INFORMATION

FOR

EVALUATION REPORT 1/2020

Uses

2,4-D is a selective herbicide. It can be used e.g. in agriculture in cereals, pastures and under fruit trees etc. and in turf to control many broadleafed weeds. The Herbicide resistance action committee categorizes 2,4-D as auxin mimic, meaning that its activity resembles that of indolyl acetic acid (IAA), a natural plant hormone (Herbicide Handbook, WSSA, 1994).

Identity of the active ingredient

ISO common name

2,4-D

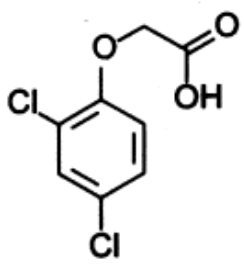
Chemical name(s)

IUPAC: (2,4-dichlorophenoxy)acetic acid
CA: (2,4-dichlorophenoxy)acetic acid

Synonyms

2,4-D Acid

Structural formula



Molecular formula

$C_8H_6Cl_2O_3$

Molar mass

221 g/mol

CAS Registry number

94-75-7

CIPAC number

1

Identity tests

Identity tests include IR/FTIR (CIPAC MT 1/TC/M3/2.2) and retention time check by HPLC (CIPAC MT 1/TC/M3/2.5)

Table 1. Physico-chemical properties of pure 2,4-D

Parameter	Value(s) and conditions	Purity %	Method reference (and technique if the reference gives more than one)	Study number
Vapour pressure	9.9×10^{-6} Pa at 20°C 2.3×10^{-5} Pa at 25°C	99.5	OECD 104, EEC A4	Study #KPN0134 Comb 2011 Nufarm
Melting point.	138.68°C	99.5	OPPTS 830.7200 EEC A1	Study #FAPC-G-10-66 Frank 2011 Dow AgroSciences
Temperature of decomposition	272.96°C	99.5	OPPTS 830.7220 EEC A2	Study #FAPC-G-10-66 Frank 2011 Dow AgroSciences
Solubility in water	0.547 g/l at 20°C purified water 3.39 g/l at 20°C pH 4 24.3 g/l at 20°C pH 7 26.5 g/l at 20°C pH 10	99.8	OPPTS 830.7840 EEC A6 OECD 105	Study #KPN0135 Comb 2011 Nufarm
Octanol/water partition coefficient	log P_{OW} = 1.54 at 20°C pH 4 log P_{OW} = -0.82 at 20°C pH 7 log P_{OW} = -1.07 at 20°C pH 10	99.8	OPPTS 830.7550 EEC A8 OECD 107	Study #KPN0136 Comb 2011 Nufarm
Hydrolysis characteristics	No hydrolysis observed in aqueous solutions buffered at pH 4- 9 at 50°C	99.6	EPA Pesticide Assessment Guidelines (Subdivision N, Section 161-1), Pea's Standard Evaluation Procedure(SEEP)	Study #5135A Cohen, Tamma, Creeger 1989 CHMR
Photolysis characteristics	Natural light, 40°N; DT_{50} 90 days pH buffer 7, DT_{50} 38 days Major metabolite: 1,2,4-benzenetriol. Max 31.7 %AR	99.5	OECD 316	Study #1002382 Lewis, Fletcher (2011c) Covance
Dissociation characteristics	pKa = 3.4 at 20°C	99.8	OPPTS 830.7370 OECD 112	Study #KPN0137 Comb 2011 Nufarm
Solubility in organic solvents	> 250 g/l methanol at 20°C 212 g/l acetone at 20°C 3.0 g/l xylene at 20°C 8.0 g/l 1,2-dichloroethane at 20°C 93 g/l ethyl acetate at 20°C 0.019 g/l heptane at 20°C	97.8	OPPTS 830.7840 EEC A6 OECD 105	Study #KPN0142 Comb 2011 Nufarm

Table 2. Chemical composition and properties of 2,4-D 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 99.8-100.2 % and percentages of unknowns were 0 %.
Declared minimum 2,4-D content	960 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them	Free phenols: maximum: 3 g/kg
Relevant impurities < 1 g/kg and maximum limits for them:	none
Stabilisers or other additives and maximum limits for them:	none

Parameter	Value and conditions	Purity %	Method reference	Study number
Melting temperature range of the TC and/or TK	138.68°C	99.5	OPPTS 830.7200 EEC A1	Study #FAPC-G-10-66 Frank 2011 Dow AgroSciences

Formulations and co-formulated active ingredients

The main formulation type for 2,4-D available is the SL (as salt). 2,4-D is can be co-formulated with many other active ingredients.

These formulations are registered and sold in many countries throughout the world.

Methods of analyis and testing

The analytical method for the active ingredient 2,4-D (including identity tests) is the AOAC-CIPAC method of analysis (1983), which uses high performance liquid chromatography. Infrared spectroscopy (IR) has been used to identify the active ingredient. The content of 2,4-D related impurities were determined by HLPC methods with UV detection and the use of internal standard. The impurities were quantified against prepared calibration standards for each impurity.

Water content was determined by Karl Fisher MT30.5.

For sulphated ash, CIPAC MT29 was used and triethanolamine insolubles were determined gravimetrically, using CIPAC MT 76.

Test methods for determination of physico-chemical properties of the technical active ingredient were according OECD, EPA and EC where appropriate.

Containers and packaging

No special requirements for containers and packaging have been identified

Expression of the active ingredient

The content of the active ingredient is expressed as 2,4-D

ANNEX 1

HAZARD SUMMARY PROVIDED BY THE PROPOSER

Notes.

(i) The proposers confirmed that the toxicological and ecotoxicological data included in the summary below were derived from 2,4-D 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 the 2,4-D technical material, based on acute toxicity, irritation and sensitization.

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Fischer 344 rats (M&F)	Oral	95	Guideline: EU B1, Doses: 500, 625, 781, 976 mg/kg b.w. by oral intubation	LD50 = 639 mg/kg b.w. for males LD50 = 764 mg/kg b.w. for females LD50 = 699 mg/kg for combined male and female	Study #490-001 1981
Sprague Dawley rats (M&F)	Oral	99.8	Guideline: EU B1 Doses: 300, 450, 675, 1000 mg/kg b.w. by oral intubation	LD50 = 559 mg/kg b.w. for males LD50 = 425 mg/kg b.w. for females	Study #SA 94109 1994
Sprague Dawley rats (M&F)	Oral	94.3	Guideline: EU B1 Doses: 300, 420, 588, 823.2, 1152.5 mg/kg b.w. by oral gavage	LD50 = 1089.6 mg/kg b.w. for males LD50 < 1089.6 mg/kg b.w. for females	Study #005961 1993
Wistar rats (F)	Oral	98.4	Guideline: OECD 432; EU B1 Doses: 300, 2000 mg/kg B.W. by oral gavage	LD50 between 300 and 2000 mg/kg b.w.	Study number: 105837 2011
NZW Rabbits (M&F)	Dermal	95	Guideline: EU B3 Duration: 14 days Doses: 2000 mg/kg b.w. by dermal application	LD50 >2000 mg/kg b.w.	Study # 490-004 1981
Sprague Dawley rats (M&F)	Dermal	99.8	Guideline: EU B3 Duration: 14 days Doses: 2000 mg/kg b.w. by dermal application	LD50 >2000 mg/kg b.w.	Study #SA 94107 1994
Sprague Dawley rats (M&F)	Dermal	94.3	Guideline: Non-guideline study Doses: 500, 750, 1125, 1687.5, 2531.3 mg/kg b.w. by dermal application	LD50 >2531 mg/kg b.w.	Study #005961 1993
Albino rabbits (M&F)	Dermal	90.6	Guideline: 870.1200 Duration: 14 days Doses: 500, 1000, 1500, 2000 mg/kg by dermal application	LD50 >2000mg/kg b.w.	Study #WIL-81233 1981
CD rat (M&F)	Inhalation	97.5	Guideline: EU B2 Duration: 14 days Doses: 1.79 mg/L by inhalation	LC50 >1.79 mg/L	Study #86-7893 1986
White Vienna rabbits (M&F)	Skin irritation	Technical	Guideline: 81-4, Fed. Reg. 38, No 83, No. 187, Section 1500.42, P.27019, Sept. 27, 1973.	Long dermal exposure to 2,4-D acid resulted in a primary irritation on rabbit skin.	Study #83/0190 1983

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
			Duration: 14 days Doses: 0.5 g/animal by dermal application		
NZW rabbits (M&F)	Skin irritation	96.7	Guideline: EU B4 Duration: 72 hours Doses: 0.5g/animal by dermal application	No dermal irritation was produced and 2,4-D was classified as non- irritant to rabbit skin	Study #K-002372-060 1992
NZW rabbits (F)	Skin irritation	99.8	Guideline: EU B4 Duration: 3 days Doses: 0.5 g/animal by dermal application	2,4-D produced a primary index irritation of 0 and was classified as non-irritant to rabbit skin	Study #SA94104 1994
NZW rabbits (M)	Skin irritation	94.3	Guideline: OECD Protocol 404, 17 July 1992. Duration: 3 days Doses: 0.5 g/animal by dermal application	No dermal irritation or corrosion were caused by 2,4-D acid technical on rabbit skin	Study #00735A 1994
White Vienna Rabbits (M&F)	Eye irritation	Technical	Guideline: 870.2400 Duration: 72 hours Doses: 0.1 ml bulk volume (66 mg of comminuted test substance) applied to conjunctival sac of the right eyelid	Severe eye irritant	Study#83/0192 1983
NZ Albino rabbits (F)	Eye irritation	99.8	Guideline: EU B5 Duration: 21 days Doses: 100 mg/animal	Classification of 2,4-D as Category 1 Eye Irritant (Irreversible effects on the eye) with the hazard statement H318 Causes serious eye damage is concluded in accordance with the EC Regulation 1272/2008 (CLP).	Study #SA 94106 1994
NZW rabbits (F)	Eye irritation	94.3	Guideline: OECD Protocol 405. Duration: 3 days Doses: 0.1 g/eye	2,4-D acid causes severe eye irritation and erosions	Study #0722B 1994
Dunkin Hartley Guinea pigs (M&F)	Skin sensitisation	99.8	Guideline: EU B6 Duration: 28 days Doses: 5% w/v by dermal application	2,4-D acid does not cause delayed contact hypersensitivity in the guinea-pig.	Study #94/0516 1994
Hartley guinea pigs (M&F)	Skin sensitization	100	Guideline: EU B6 Duration: 5 weeks Doses: 5% w/v by dermal application	2,4-D is classified as a non-sensitizing agent in guinea pigs.	Study#2184-105 1986

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Dunkin-Hartley Guinea pigs (M&F)	Skin sensitization	94.3	Guideline: Magnusson and Klingman method Duration: 3 weeks Doses: 0.2 ml of 50% 2,4-D	2,4-D acid exhibited no clear sensitizing potential, since symptoms of extreme allergenicity potential were observed in both control and test animals	Study #00738C 1994
Mice (F)	Skin sensitization	99.7	Guideline: OECD 429 Duration: 8 days Doses: 10, 25 and 50% w/v 2,4-D in DMF by epidermal application	Based on the results of the LLNA study, 2,4-D was not found to be a skin sensitizer.	Study number: 1368600; R-90013957 2011

Table 4. Toxicology profile of 2,4-D technical material based on repeated administration (subacute to chronic)

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Fischer 344 rats (M&F)	Sub-chronic oral toxicity	96.1	Guideline: 870.3100 Duration: 90 days Doses: 0, 1, 15, 100, 300 mg/kg/day by diet Findings: Clinical chemistry, hematology and histology changes	NOAEL = 15 mg/kg bw/d LOAEL = 100 mg/kg bw/d	Study #2184-116 1991a
B6C3F1 mouse (M&F)	Sub-chronic oral toxicity	96.1	Guideline: 870.3100 Duration: 90 days Doses: 0, 1, 15, 100, 300 mg/kg/day by diet Findings: Kidney changes	NOAEL = 15 mg/kg/day LOAEL = 100 mg/kg/day	Study #2184-117 1991b
Beagle Dogs (M&F)	Subchronic oral (capsule) toxicity	96.1	Guideline: 870.3150 Duration: 90 days Doses: 0, 0.3, 1.0, 3.0, and 10 mg/kg/day by diet (gelatin capsules) Findings: Toxic signs and increased BUN level	NOAEL = 1 mg/kg/day LOAEL = 3 mg/kg/day	Study #2184-115 1990a
Beagle Dogs (M&F)	Subchronic oral (diet) toxicity	96.7	Guideline: 870.3150 Duration: 90 days Doses: 0, 0.5, 1.0, 3.75 and 7.5 mg/kg/day by diet Findings: Increased levels of ALT, creatinine, and albumin	NOAEL = 1 mg/kg/day LOAEL = 3.75 mg/kg/day	Study #2184-125 1993a
Rabbit (M&F)	Dermal toxicity	96.1	Guideline: 870.3200 Duration: 21 days Doses: 0, 10, 100, 1000 mg/kg/day by dermal application Findings: Effects on absolute and relative kidney weight	NOAEL = 1000 mg/kg/day LOAEL = 1000 mg/kg/day	Study #2184-106 1990 Study #2184-109 1990b
Sprague Dawley CD rats (M&F)	Inhalation toxicity	99	Guideline: 870.3465 Duration: 28 days Doses: 0, 0.05, 0.1, 0.3, 1.0 mg/L by nose-only inhalation Findings: Squamous metaplasia of larynx	Systemic NOAEL = 0.3 mg/L/day Systemic LOAEL = 1.0 mg/L/day	Study #07-6156 2008
Fischer 344 rats (F)	Developmental toxicity	97.5	Guideline: 870.3700; GD 6-15 Duration: 21 Days Doses: 0, 8, 25, and 75 mg/kg/day by oral administration Findings: maternal toxicity and fetotoxicity	Maternal NOAEL = 25 mg/kg/day Maternal LOAEL = 75 mg/kg/day Developmental NOAEL = 25 mg/kg/day	Study #WIL-81135 1983

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
				Developmental LOAEL = 75 mg/kg/day	
New Zealand White rabbit (F)	Prenatal developmental	96.1	Guideline: 870.3700b, GD 6-18 Duration: 21 days Doses: 0, 10, 30, and 90 mg/kg/day by stomach tube Findings: Maternal toxicity, No embryotoxic/fetotoxic effect	Maternal NOAEL = 30 mg/kg/day Maternal LOAEL = 90 mg/kg/day Developmental NOAEL = 30 mg/kg/day Developmental LOAEL = 90 mg/kg/day	Study #320-003 1990
Fischer 344 rats (M&F)	2 generation reproduction and fertility effects	97.5	Guideline: 870.3800 Doses: 0, 5, 20, and 80 mg/kg/day by diet Findings: Parental-reduced female body weight, microscopic findings in the kidney Reproductive-increased gestation period, reduced fertility indices and reduced offspring survival Offspring-increased incidence of skeletal and visceral variations, clinical signs	Parental NOAEL = 5 mg/kg/day Parental LOAEL = 20 mg/kg/day Reproductive NOAEL = 20 mg/kg/day Reproductive LOAEL = 80 mg/kg/day Offspring NOAEL = 5 mg/kg/day Offspring LOAEL = 20 mg/kg/day	Study #WIL-81137 1985 (original) 1986 (addendum)
Crl:CD(SD) rat (M&F)	Extended One Generation Reproductive toxicity (EOGRT)	97.85	Guideline: 870.3800 and OECD 443 and 416 Doses: 0, 100, 300 and 600 ppm (females) or 800 ppm (males) by diet Findings: Parental-decreased body weight during lactation, kidney effects, reduced kidney weight and degenerative lesions in the kidney Reproductive-no effects Offspring-kidney effects, reduced kidney weight and degenerative lesions in the kidney	Parental (male) systemic NOAEL= 16.6 mg/kg/day Parental (male) systemic LOAEL = 45.3 mg/kg/day Parental (female) systemic NOAEL= 40.2 mg/kg/day Thyroid toxicity(male) NOAEL=45.3 mg/kg/day Thyroid toxicity(female) NOAEL=40.2 mg/kg/day Offspring (F1 adult male) NOAEL = 20.9 mg/kg/day Offspring (F1 adult female) NOAEL = 23.3 mg/kg/day Offspring (F1 adult male) LOEL = 55.6mg/kg/day	Study #081104 2010 Summary document prepared but not submitted to EPA; see reference list

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
				Offspring (F1 adult female) LOAEL = 46.7 mg/kg/day F1 offspring NOAEL = 300 ppm. F1 offspring LOAEL = 800/600 ppm. DNT offspring (male) NOAEL = 81.7 mg/kg/day DNT offspring (female) NOAEL= 59.2 mg/kg/day. DIT offspring(male) NOAEL = 71.8 mg/kg/day DIT offspring(female) = 55.3 mg/kg/day. Reproductive (male) NOAEL = 45.3 mg/kg/day Reproductive (female) NOAEL = 40.2 mg/kg/day	
Fischer 344 rat (M&F)	Chronic toxicity, Carcinogenicity	96.1	Guideline: 870.4100a 870.4200 Duration: 24 months Doses: 0,5,75,or 150 mg/kg/day by diet Findings: clinical chemistry, hematology and histopathology alterations in liver, thyroid, and kidneys	NOAEL = 5 mg/kg bw/d (males and females) LOAEL = 75 mg/kg bw/d (females); 150 mg/kg/day (males)	Study #K-002372-064F 1995
Fischer 344 rat (M&F)	Chronic neurotoxicity	96.6	Guideline: FIFRA 83-1 Duration: 12 months Doses: 0, 5, 75, 150 mg/kg b.w./day/dietary Findings: bilateral retina degeneration in high dose females, increased urination in high dose females	NOAEL = 5 mg/kg b.w./day	Study #K-002372-064N 1994
Beagle dog (M&F)	Chronic toxicity	96.7	Guideline: 870.4100b Duration: 52 weeks Doses: 0, 1, 5, 7.5/10 mg/kg/day by diet Findings: clinical chemistry and histopathological findings	NOAEL = 1 mg/kg bw/d LOAEL = 5 mg/kg bw/d	Study #2184-124 1993c
B6C3F1 CRL BR mouse	Carcinogenicity	97.5	Guideline: 870.4300 Duration: 104 weeks	NOAEL = 1 mg/kg bw/d LOAEL = 15mg/kg bw/d	Study #2184-101 1987

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
(M&F)			Doses: 0, 1, 15, or 45 mg/kg/day by diet Findings: Kidney effects		
B6C3F1 CRL BR mouse (M&F)	Carcinogenicity	96.4	Guideline: 870.4300 Duration: 104 weeks Doses: 0, 5, 62/150, or 120/300 mg/kg/day (male/female) by diet Findings: Kidney effects	NOAEL = 5 mg/kg bw/d LOAEL = 62/150 mg/kg bw/d (male/female)	Study #K-002372-063F (female) 1995 Study #K-002372-063M (male) 1995a
Fischer 344 rat (M&F)	Acute neurotoxicity	96.1	Guideline: 870.6200a Doses: 0, 15, 75, or 250 mg/kg/day by oral gavage Findings: Changes in gait, coordination, and locomotion	NOAEL = 67 mg/kg bw/d LOAEL = 227 mg/kg bw/d	Study #K-002372-066 1994a
Fischer 344 rat (M&F)	Subchronic neurotoxicity	96.45	Guideline: 870.6200b Duration: 23 months Doses: 0, 5, 75, 150 mg/kg/day by diet Findings: bilateral retina degeneration in high dose females, increased urination in high dose females	NOAEL = 71/68 mg/kg bw/d (M&F) LOAEL = 141/139 mg/kg w/d (M&F)	Study #K-002372-064N 1994b
Crl:CD(SD)rat (M&F)	Developmental neurotoxicity	97.85	Guideline: 870.6300 Doses: 0, 100, 300 and 600 ppm (females) or 800 ppm (males) by diet Findings: No evidence of developmental neurotoxicity	DNT offspring (male) NOAEL = 81.7 mg/kg/day DNT offspring (female) NOAEL= 59.2 mg/kg/day.	Study #081104 2010
Rat uterine cytosol	Estrogen Receptor Binding Assay	98.5	Guideline: OCSPP 890.1250 Dose: 10-11 to 10-4 M	Classified as Not Interactive	Study #111121 2011
Human cell line HeLa 9903	Estrogen Receptor Transcriptional Activation Assay	98.5	Guideline: OCSPP 890.1300 Doses: 10-10 to 10-4 M	Negative for estrogen receptor transcriptional activation	Study #111043 2011
Rat prostate cytosol	Androgen Receptor Binding Assay	98.5	Guideline: OCSPP 890.1150 Doses: 10-11 to 10-4 M	Classified as a non-binder	Study #111111 2011
Human cell line H295R	Steroidogenesis Assay	98.5	Guideline: OCSPP 890.1550 Duration: 48 hours Doses: 10-10 to 10-4 M	2,4-D treatment resulted in statistically significant and reproducible increases in	Study #111038 2011

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
				estradiol production at the highest dose tested. 2,4-D treatment did not result in statistically significant and reproducible alterations in testosterone production.	
Human recombinant microsomes	Aromatase Assay	98.5	Guideline: OCSPP 890.1200 Doses: 10-11 to 10-4 M	Classified as a Non-inhibitor of aromatase activity	Study #111036 2011

Table 5. Mutagenicity profile of 2,4-D 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, TA 1535, TA 1537, TA1538	Bacterial reverse mutation test	96.1	Guideline: 870.5100 Doses: 100-1000 µg/plate w/S9; 66.7-6670 µg/plate w/out S9	No evidence of bacterial mutation w/ and w/out S9	Study #10979-0-401 1990
Rat hepatocytes	Unscheduled DNA synthesis assay	96.1	Guideline: 870.5450 Doses: 2890 µg/ml to 0.969 µg/ml	No evidence of induction of unscheduled DNA synthesis	Study #10979-0-447 1990
ICR mouse (bone marrow)	*In vivo* mouse micronucleus assay	96.1	Guideline: 870.5395 Doses: 40-400 µg/kg by oral gavage	No significant increase in frequency of micronucleated polychromatic erythrocytes in bone marrow at any time point	Study #10979-0-455 1990 (original and supplemental studies)
Salmonella typhimurium	Bacterial reverse mutation assay	98.4	Guideline: EC Directive 2000/32/EC, Method B.13/14, OECD Guideline 471. Doses: 31.6, 100, 316, 1000, 3160 µg/plate	No mutagenic effect in the *Salmonella typhimurium* strains TA 98, TA 100, TA 102, TA 153 and TA 1537 in the plate incorporation or pre-incubation tests carried out with and without metabolic activation.	Study #24810 2009a
NMRI mouse (M&F)	Micronucleus test by oral administration	98.4	Guideline: OECD Guidelines for Testing of Chemicals “Mammalian Erythrocyte Micronucleus Test” (No. 474, July 21, 1997). Doses: 30, 60, 125, 200, 250, 500, 1000, 2000 mg/kg/day	2,4-D tested up to the dose level of 200 mg/kg b.w. by oral administration showed no mutagenic properties in the mouse bone marrow micronucleus study at the two tested sampling times of 24 hours and 48 hours.	Study #24809 2009b
CHO/HPRT	Mutagenicity in the *in vitro* mammalian cell mutation assay	98.71	Guideline: EC, B. 17 (2008); OECD, Guideline 476 (1997). Doses: 0, 125, 250, 500, 1000, 2210 µg/ml in the absence of S9 and 0; and 500, 1000, 1200, 1400, 1600, 1800, 2000, 2210 ug/ml in the presence of S9	The test article was non-mutagenic when evaluated in the absence or presence of a metabolic activation (S9) system up to precipitating dose levels.	Study #131053 2013

Table 6. Ecotoxicology profile of 2,4-D technical material

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Mallard duck	Avian acute oral toxicity	96.1	Guideline: 850.2100 Duration: 8 days Doses: 562, 1000, 1780, 3160 and 5620 ppm a.i. by diet	LC50 >5620 mg ae/KG	Study #103-307 1990
Japanese quail	Avian acute oral toxicity	98	Guideline: 850.2100 Duration: 14 days Doses: 0, 190, 305, 488, 781, 1250 mg/kg b.w.	LD50 = 617.3 mg/kg b.w.	Study #G/64/03 2004
Canary	Avian acute oral toxicity	99.5	Guideline: 850.2100 Duration: 14 days Doses: 0, 105, 175, 292, 486, 810 mg/kg b.w.	LD50 = 633 mg ae/kg b.w.	Study #379-239 2011
Canary	Avian acute oral dietary toxicity	98.14	Guideline: 850.2200 Duration: 8 days Doses: 0, 1100, 1650, 2500, 3700, 5600 by diet	LC50 >4790 mg ae/kg-diet	Study #467-118 2014
Northern Bobwhite quail	Avian subacute dietary toxicity	96.1	Guideline 850.2200 Duration: 5 days Doses: 562, 1000, 1780, 3160, 5620 ppm by diet	LC50 >5620 mg ae/kg-diet NOEC = 3620 ppm	Study #103-306 1990
Mallard duck	Avian subacute dietary toxicity	96.1	Guideline: 850.2200 Duration: 5 days Doses: 562, 1000, 1780, 3160, 5620 ppm by diet	LC50 >5620 mg ae/kg-diet NOEC >5620 ppm	Study #103-307 1990
Northern Bobwhite quail	Avian reproduction	96.9	Guideline: 850.2300 Duration: 21 weeks Doses: 0, 160, 400, 1000 ppm by diet	NOEC/LOEC 962/>962 ppm	Study #467-106 2000
Japanese quail	Avian reproduction	98	Guideline: OECD Guideline No 206 (1984). Duration: 20 weeks Doses: 40, 200 and 1000 mg/kg.	NOEC = 1000 mg/kg diet	Study #G/17/03 2004
Rainbow trout	Acute toxicity Freshwater fish	98.7	Guideline: 850.1075 Duration: 96 hours Doses: 204-500 mg/L	LC50 = 358 mg ae/L	Study #ES-DR-0002-2297-4 1983
Bluegill sunfish	Acute toxicity Freshwater fish	98.7	Guideline: 850.1075 Duration: 96 hours Doses: 204-500 mg/L	LC50 = 263 mg ae/L	Study #ES-DR-0002-2297-4 1983
Fathead minnow	Acute toxicity Freshwater fish	98.7	Guideline: 850.1075 Duration: 96 hours Doses: 204-500 mg/L	LC50 = 320 mg ae/L	Study #ES-DR-0002-2297-4 1983
Common carp	Acute toxicity Freshwater fish	98	Guideline: 850.1075 Duration: 96 hours.	LC50 = 239.9 mg/L	Study #W/56/03 2004

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
			Doses: Common carp: 100, 180, 320 mg/l.		
Rainbow trout	Acute toxicity Freshwater fish	98	Guideline: 850.1075 Duration: 96 hours. Doses: Rainbow trout: 32, 56, 100, 180, 320 mg/l;	LC50 = 239.9 mg/L	Study #W/56/03 2004
Daphnia magna	Freshwater invertebrate acute toxicity	98.7	Guideline: 850.1075 Duration: 48-hour Doses: 12-100 mg/L	LC50 = 25 mg ae/L	Study #ES-DR-0002-2297-4 1983
Daphnia magna	Freshwater invertebrate acute toxicity	98	Guideline: OECD Guideline 202, Part I. Duration: 48 hours Doses: 32, 56, 100, 180, 320 mg/L	EC50 = 134.3 mg/L	Study #W/22/03 2003
Eastern oyster	Estuarine/ Marine invertebrate acute toxicity	95.1	Guideline: 850.1025 Duration: 96 hours Doses: 0, 29, 48, 76, 110 and 190 mg/L	EC50 = 57 mg ai/L	Study #286-DE 1993
Tidewater silverside	Estuarine/ Marine acute toxicity-fish	96.1	Guideline: 850.1075 Duration: 96 hours Doses: 0, 104, 173, 288, 480, 800 mg/L	LC50 = 175 mg ae/L	Study #3903008000-0210-3140 1990
Pink Shrimp	Estuarine/ Marine invertebrate acute toxicity	96.1	Guideline: 850.1045 Duration: 96 hours Doses: 0, 104, 173, 288, 480, 800 mg/L	LC50 = 467 mg ae/L NOEC = 187 mg/L	Study #3903008000-0200-3140 1990
Fathead minnow	Freshwater Fish Early Life Stage Toxicity	96.1	Guideline: 850.1300 Duration: 32 days Doses: 12.6, 22.2, 37.4, 63.4, 101.5 mg/L	NOEC = 63.4 mg/L LOEC <102 mg ae/L MATC = 80.4 ppm	Study #ES-DR-0002-2297-10 1990
Rainbow trout	Chronic toxicity test on juvenile fish	98	Guideline: OECD Guidelines 215. Duration: 28 days Doses: 0.10, 0.32, 1.00, 3.20, 10.0 mg/l.	NOEC = 7.21 mg/L	Study #W/24/03 2004
Zebra fish	Freshwater Fish Early Life Stage Toxicity	98	Guideline: OECD Guidelines 210. Duration:28 days. Doses: 10.0 mg/l.	NOEC > 10 mg/L LOEC > 10 mg/L	Study #W/25/03 2004
Daphnia magna	Freshwater aquatic invertebrate life cycle	91.3	Guideline: 850.1300 Duration: 21 days Doses: 0, 112, 192, 320, 472, 800 mg/L	NOEC = 79 mg/L LOEC = 151 mg ae/L MATC = 109 mg ae/L EC50 = 235 mg/L	Study #9040-D 1991
Daphnia magna	Freshwater aquatic invertebrate reproduction study	98	Guideline: OECD Guideline 211. Duration: 21 days. Doses: 32, 56, 100, 180, 320 mg/l.	NOEC = 100mg/L	Study #W/23/03 2003

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Leopard frog tadpoles	Freshwater amphibian acute toxicity	97.5	Guideline: 850.3020 Duration: 96 hours Doses: 65, 108, 180, 300, 500 mg/L	LC50 = 359 mg ae/L	Study #467A-102 1997
South African Clawed Frog	Amphibian Metamorphosis assay	98.6	Guideline: 890.1100 Duration: 21 days Doses: 0, 0.273, 3.24, 38.0, 113 mg/L	NOEC = 113 mg/L	Study #101025 2010
Fathead minnow	Fish short term reproduction assay	98.6	Guideline: 890.1350 Duration: 21 days Doses: 0, 0.245, 3.14, 34.0, 96.5 mg/L	Throughout the exposure, there was only one incidence of fish mortality and no indications of treatment related abnormal behaviour or appearance. No significant differences between control and 2,4-D exposed fish were observed in regard to fertility, male and female wet weight and length, gonadal somatic indices, tubercle scores, or blood plasma concentrations of VTG in either male or female fish. Furthermore, there were no treatment-related histopathologic changes in the testes or ovaries in any of the 2,4-D exposed dose-groups. The only significant effect compared to the controls that was observed in the present study was a decrease in fecundity among fish exposed to the highest concentration of 96.5 mg/L 2,4-D. Since there were no significant treatment related effects on the more specific endocrine-responsive endpoints, such as vitellogenin concentrations,	Study #101026 2010

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
				gonadal-somatic indices, gonadal histopathology or tubercle scores, it is likely that the observed decrease in fecundity at the highest concentration tested is a generalized stress response which is not necessarily linked to an endocrine specific mode of action in the hypothalamus-pituitary-gonadal (HPG) axis of the exposed fish.	
Lemna gibba	Nontarget aquatic plant toxicity	96.2	Guideline: 850.4400 Doses: 62.5, 125, 249, 500, 1000, 2000 ug a.i./L	EC50/NOEC = 0.695/0.0581 mg ai/L	Study #10-05-1 1997
Lemna minor	Nontarget aquatic plant toxicity	98	Guideline: OECD Guideline 221. Duration: 7-day Doses: 0.32, 1.0, 3.2, 10, 32, 100 mg/L	EyC50/ErC50 = 10.66/17.51 mg/L (frond numbers) EyC50 18.50 mg/L and ErC50 > 100 mg/L (dry weight	Study #W/57/03 2004
Selenastrum capricornutum	Nontarget aquatic plant toxicity	96.1	Guideline: 850.5400 Duration: 120 hours Doses: 6.19, 12.4, 24.8, 49.5, 99.1 mg/L	NOEC = 26.4 mg ae/L	Study #0460-05-1100-1 1990
Anabaena flos-aquae	Nontarget aquatic plant toxicity	96.9	Guideline: 850.4400 Duration: 5 days Doses: 2 mg/L	>2.02 mg ae/L	Study #10-01-1 1994
Navicula pelliculosa	Nontarget aquatic plant toxicity	96.9	Guideline: 850.4400 Duration: 5 days Doses: 2 mg/L	>2.13 mg ae/L	Study #10-01-2 1994
Skeletonema costatum	Nontarget aquatic plant toxicity	96.9	Guideline: 850.5400 Duration: 5 days Doses: 2 mg/L	2.08 mg ae/L	10-01-3 43307903 1994
Pseudokirchneriella subcapitata	Nontarget aquatic plant toxicity	99.5	Guideline: OECD Guidelines 201. Duration: 72 hours Doses: 2.5, 5.0, 10, 20, 40, 80 mg/L	EyC50 and ErC50 < 78 mg/L NOEC = 39 mg/L	Study #379A-148A 2011
Navicula pelliculosa	Nontarget aquatic plant toxicity	99.5	Guideline: OECD Guildeline 201. Duration: 72 hours Doses: 0, 0.324, 0.941, 3.04, 9.85, 29.7, 98.7 mg/L	ErC50 and EyC50 > 100mg/L NOEC = 100 mg/L	Study #67558 2011

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
Scenedesmus subspicatus	Nontarget aquatic plant toxicity	98	Guideline: OECD Guideline 201. Duration: 72 hours Doses: 0, 10, 32, 100, 320, 1000 mg/L	EC50 >582.2 mg/L	Study #W/55/03 2004
Skeletonema costatum	Nontarget aquatic plant toxicity	98	Guideline: OECD Guidelines 201. Duration: 120 hours Doses: 0, 0.032, 0.10, 0.32, 1.0, 3.2 mg/L	EyC50 / ErC50 0.68/4.58 mg/L NOEC <0.032 mg/L LOEC = 0.032 mg/L	Study #W/24/04 2005
Skeletonema costatum	Nontarget aquatic plant toxicity	99.5	Guideline: OECD Guideline 201, EU Directive 92/69/EEC, Method C.3. Duration: 72 hours Doses: 6.3, 13, 25, 50, 100 mg/L	EyC50 and ErC50 > 101 mg/L NOAEC = 13 mg/L	Study #379A-150A 2011
Anabaena flos-aquae	Nontarget aquatic plant toxicity	98	Guideline: OECD Guidelines 201. Duration: 72 hours. Doses: 1.0, 3.2, 10, 32, 100 mg/l.	EyC50 and ErC50 > 100mg/L	Study #W/24/04 2005
Honeybee	Brood Feeding test	99.1	Guideline: Oomen et al (1992) Duration: 21 days Doses: 1, 5, 53, 265 mg/kg	2,4-D technical did not adversely affect honey bee brood development NOEC 265 ppm	Study #64731031 2012
Earthworm	Reproduction test	98	Guideline: PN-ISO 11268-2. PN-Duration: 28 days Doses: 0, 62.5, 125, 250, 500, 100 mg/kg dry weight soil	EC50 = 135.2 mg/kg dry soil LOEC = 125 mg/kg dry soil NOEC = 62.5 mg/kg dry soil	Study #G/63/03 2004
Activated sludge microorganisms	Respiration inhibition test	99.5	Guideline: OECD 209, EEC C.11. Duration: 3 hours Doses: 0.1, 1, 10, 100, 1000 mg a.s./L	EC50 >1000mg/L	Study #379E-102 2011

The IPCS hazard classification of 2,4-dichlorophenoxyacetic acid is: class 9. (www.inchem.org/documents/icsc/icsc/eics0033.htm)

European Chemicals Agency List No.:202-361-1 CAS No.: 94-75-7: *Danger!* According to the harmonised classification and labelling approved by the European Union, this substance is harmful if swallowed, causes serious eye damage, is harmful to aquatic life with long lasting effects, may cause an allergic skin reaction and may cause respiratory irritation. (https://echa.europa.eu/substance-information/-/substanceinfo/100.002.147)

International Agency for Research on Cancer: Monograph 113, 14 September 2016. There is inadequate evidence in humans for the carcinogenicity of 2,4-dichlorophenoxyacetic acid (2,4-D). There is limited evidence in experimental animals for the carcinogenicity of 2,4-dichlorophenoxyacetic acid (2,4-D). 2,4-dichlorophenoxyacetic acid (2,4-D) is possibly carcinogenic to humans (Group 2B) (http://monographs.iarc.fr/ENG/Monographs/vol113/index.php)

ANNEX 2

REFERENCES

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