Food and Agriculture Organization
of the United Nations

FAO SPECIFICATIONS AND EVALUATIONS

FOR AGRICULTURAL PESTICIDES

2,4-D

(2,4-dichlorophenoxy)acetic acid

2020

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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 that 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 5th edition of the "Manual on the development and use of FAO specifications for plant protection products" and later in the 1st edition of "Manual for Development and Use of FAO and WHO Specifications for Pesticides" (2002) - currently available as 3rd revision of the 1st edition (2016) - , 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 1999 onwards the publication of FAO specifications under the **New Procedure** has changed. Every specification consists now of two parts namely the specifications and the evaluation report(s):

Part One: **The Specification** of the technical material and the related formulations of the pesticide in accordance with chapters 4 to 9 of the "Manual on development and use of FAO and WHO specifications for pesticides".

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

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

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

PART ONE
SPECIFICATION

2,4-D

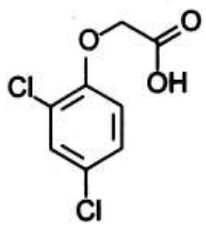
INFORMATION

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

Chemical names
IUPAC (2,4-dichlorophenoxy)acetic acid
CA (2,4-dichlorophenoxy)acetic acid

Synonym
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 comparison of retention times of the chromatographic signals for a 2,4-D standard and a sample in HPLC (CIPAC MT 1/TC/M3/2.5)

2,4-D TECHNICAL MATERIAL

FAO Specification 1 / TC (September 2020)

*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 report (*1/2020). *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 specifications. The specification may not be appropriate for TC produced by other manufacturers. The evaluation report (*1/2020*), as PART TWO, forms 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, 1985)

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 these compounds expressed as 2,3,7,8-tetrachlorodibenzodioxin (2,3,7,8-TCDD) toxic equivalents (TEQ) exceed 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.

PART TWO

EVALUATION REPORT

2,4-D

2,4-D
FAO/WHO EVALUATION REPORT 1/2020

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 Jiangxi Tianyu Chemical Co., Ltd. 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

FAO "old procedure" specifications for 2,4-D and variants have been developed and published (1984 for the TC - (1/TC/S/F (1992)), sodium salts (1.1Na/TC/S/F (1992)) and 1992 and 1994 for the esters (1.3/TC/S/F (1992)). 2,4-D was qualified as a candidate for conversion of an old procedure into a new procedure specification[2]. 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 1996. [JMPR, 1996].

The Meeting considered data for 2,4-D were evaluated in support of the conversion of the old procedure FAO specifications. The draft specification for 2,4-D TC and the supporting data provided by the Industry Task Force II on 2,4-D Research Data (members: 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[3] that the name of the company had changed to Jiangxi Tianyu Chemical Co., Ltd. This name change has been noted by FAO.

[2] see http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Specs/Call_for_data.pdf (September 2020)
[3] 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.

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. [Margerison], [Karassali, 1], [Karassali, 2], [Bressant], [Kielek]

2,4-D is a white crystalline powder. It has a rather low volatility and a melting point of 138.68 °C. 2,4-D is moderately soluble in unbuffered water, however solubility is strongly pH-dependent and increases up to 26.5 g/l in pH 10 buffered water. It is readily soluble in a number of organic solvents. The log P_{ow} at pH 7 is -0.82. 2,4-D as a carboxylic acid 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 to 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 LD50 for 2-CPA and the geometric mean of the 2,4-D LD50 – 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) 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 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

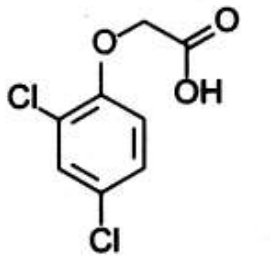
ISO common name 2,4-D (ISO 1750, published)

Chemical names

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

Synonym 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 comparison of retention times of the chromatographic signals for a 2,4-D standard and a sample in 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; DT50 90 days pH buffer 7, DT50 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

Parameter	Value(s) and conditions	Purity %	Method reference (and technique if the reference gives more than one)	Study number
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	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 has been determined by Karl Fisher MT30.5.

For sulphated ash, CIPAC MT29 has been 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 Error! Bookmark not defined.
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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number Error! Bookmark not defined.
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. Duration: 14 days Doses: 0.5 g/animal by dermal application	Long dermal exposure to 2,4-D acid resulted in a primary irritation on rabbit skin.	Study #83/0190 1983
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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number Error! Bookmark not defined.
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 Error! Bookmark not defined.
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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
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 Developmental LOAEL = 75 mg/kg/day	Study #WIL-81135 1983
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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
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 Offspring (F1 adult female) LOAEL = 46.7 mg/kg/day F1 offspring NOAEL = 300 ppm. F1 offspring LOAEL = 800/600 ppm.	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
				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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
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 (M&F)	Carcinogenicity	97.5	Guideline: 870.4300 Duration: 104 weeks Doses: 0, 1, 15, or 45 mg/kg/day by diet Findings: Kidney effects	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
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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
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 estradiol production at the highest dose tested. 2,4-D treatment did not result in statistically significant and reproducible alterations in testosterone production.	Study #111038 2011
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
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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
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

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
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

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: 100-1000ug/plate w/S9; 66.7-6670 ug/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 ug/ml to 0.969 ug/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 ug/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 ug/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).	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	Study #24809 2009b

Species	Test	Purity %	Guideline, duration, doses and conditions	Result	Study number
			Doses: 30, 60, 125, 200, 250, 500, 1000, 2000 mg/kg/day	sampling times of 24 hours and 48 hours.	
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 ug/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. Doses: Common carp: 100, 180, 320 mg/l.	LC50 = 239.9 mg/L	Study #W/56/03 2004
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.	NOEC > 10 mg/L LOEC > 10 mg/L	Study #W/25/03 2004

			Doses: 10.0 mg/l.		
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
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	Study #101026 2010

				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, 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	ErC50 and EyC50 > 100mg/L NOEC = 100 mg/L	Study #67558 2011

			Doses: 0, 0.324, 0.941, 3.04, 9.85, 29.7, 98.7 mg/L		
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.	EC50 = 135.2 mg/kg dry soil LOEC = 125 mg/kg dry soil	Study #G/63/03 2004

			PN-Duration: 28 days Doses: 0, 62.5, 125, 250, 500, 100 mg/kg dry weight soil	NOEC = 62.5 mg/kg dry soil	
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 Schaefer et al 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

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
IPCS, 1984		1984	http://www.inchem.org/documents/ehc/ehc/ehc29.htm#PartNumber:9
IPCS, 1987		1987	http://www.inchem.org/documents/hsg/hsg/hsg005.htm
JMPR, 2001		2001	http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Reports_1991-2006/REPORT2001.pdf, p.43
JMPR, 2017		2017	http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Report2017/5.9_2_4-D__020_.pdfhttp://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Report2017/5.9_2_4-D__020_.pdf
EPA, 2005		2005	https://archive.epa.gov/pesticides/reregistration/web/pdf/24d_red.pdf
CIR, 2015		2015	https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2015.298.01.0008.01.ENG&toc=OJ:L:2015:298:TOC
HC, 2017		2017	https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/decisions-updates/reevaluation-note/2017/rev2017-08-re-evaluation-note-update-2-4-d.html
AGP: CP/100		1984	http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-old/en/
AGP:CP/310		1994	http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-old/en/
FAO/WHO Manual		2016	http://www.fao.org/3/a-i5713e.pdf
Margerison		2019	E-mail from Samuel Margerison, sent on 16 April 2019, 11:54:46 AM [From samuel.margerison@apvma.gov to laszlo.bura@efsa.europa.eu]
Karassali, 1		2019	E-mail from Καρασαλή Ελένη, sent on 16 April 2019, 11:54:46 AM [From: e.karassali@bpi.gr to laszlo.bura@efsa.europa.eu] (Dow)
Karassali, 2		2019	E-mail from Καρασαλή Ελένη, sent on 16 April 2019, 12:23:44 PM [From: e.karassali@bpi.gr to laszlo.bura@efsa.europa.eu] (Nufarm)
Bressant		2019	E-mail from Bressant Janet, sent on 25 April 2019, 11:58:34 AM [From: Bressant.Janet@epa.gov to laszlo.bura@efsa.europa.eu]
Kielek		2019	E-mail from Przemyslaw Kielek, sent on 13 July 2019 9:13 [From: przemyslaw.kielek@minrol.gov.pl to laszlo.bura@efsa.europa.eu]
JMPR, 1996		1996	http://www.inchem.org/documents/jmpr/jmpmono/v96pr04.htm
CIPAC, F	Martijn A and Dobrat W	1995	CIPAC Handbook Volume F. Physico-chemical Methods for Technical and Formulated Pesticides
CIPAC, J	Martijn A and Dobrat W	2000	CIPAC Handbook Volume J. Analysis of Technical and Formulated Pesticides

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
CIPAC, 1C	Henriet J, Martijn A and Povlsen H.H	1985	CIPAC Handbook Volume 1C. Analysis of Technical and Formulated Pesticides
KPN0134		2011	2,4-D pure Vapour pressure and Calculation of Volatility(Henry's Law Constant) Study KPN0134. Report KPN0134 GLP. Unpublished
FAPC-G-10-66		2011a	Determination of melting point and decomposition temperature of 2,4-D acid pure active ingredient. Study Number FAPC-G-10-66. GLP. Dow AgroSciences LLC. USA. Unpublished.
KPN0135		2011	2,4-D pure Water Solubility. Study KPN0135. Report KPN0135 GLP. Unpublished
KPN0136		2011	2,4-D pure Partition Coefficient. Study KPN0136. Report KPN0136 GLP. Unpublished
5135A		1989	Hydrolysis of 2,4-D in aqueous solutions buffered at pH 5, 7, and 9. Study Number 5135A. GLP. Unpublished
1002382		2011c	[14C] 2,4-D: Photodegradation and Quantum Yield in Sterile pH 7 Buffer and Natural Water. Study number: 1002382. GLP, Unpublished
KPN0137		2011	2,4-D pure Dissociation Constant. Study KPN0137. Report KPN0137 GLP. Unpublished
KPN0142		2011	2,4-D Technical Solvent Solubility. Study KPN0142. Report KPN0142 GLP. Unpublished.
490-001		1981	Determination of Acute Oral LD50 in Fischer 344 Rats (2,4-Dichlorophenoxyacetic acid, technical). Study Number 490-001. GLP. Unpublished.
SA 94109		1994	2,4-D-Acute Oral LD50 in the rat. Study number: SA 94109. GLP. France. Unpublished
005961		1993	Oral and Dermal LD_{50} tests with Sanachem Sanaphen-D (2,4-D Acid Technical) in rats. Study Number: 005961. GLP. Unpublished
005961		1993	Oral and Dermal LD_{50} tests with Sanachem Sanaphen-D (2,4-D Acid Technical) in rats. Study Number: 005961. GLP. Unpublished
105837		2011	Acute Oral Toxicity (Acute Toxic Class Method) with 2,4-D Acid. Study number: 105837. GLP. Unpublished
490-004		1981	2,4-Dichlorophenoxyacetic acid technical Determination of Acute Dermal LD50 in Fischer 344 Rats. Study number: 490-004. GLP. Unpublished
SA 94107		1994	2,4-D-Acute Dermal LD50 in the rat. Study number: SA 94107. GLP. Unpublished
WIL-81233		1981	Acute Dermal Toxicity Study in Albino Rabbits with ITF-5; 2,4-Dichlorophenoxyacetic Acid, Sodium Salt. Study Number WIL-81233. GLP. USA. Unpublished
86-7893		1986	An Acute Inhalation Toxicity Study of 2,4-Dichlorophenoxyacetic Acid in the Rat. Study Number 86-7893. GLP. Unpublished.
83/0190		1983	Report on the study of the irritation to the intact and abraded dorsal skin of the white rabbit based on Draize of 2,4-D. Study number: 83/0190. GLP.. Germany. Unpublished.
K-002372-060		1992	2,4-Dichlorophenoxyacetic Acid: Primary Dermal Irritation Study in New Zealand White Rabbits. Study Number K-002372-060. GLP. Unpublished.

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
SA 94104		1994	2,4-D-Acute dermal irritation test in the rabbit. Study number: SA 94104. GLP. Unpublished
00735A.		1994	Acute dermal irritation and corrosion tests with Sanachem 2,4-D amine 480 g/L in rabbits. Study Number: 00735A. GLP. Unpublished
83/0192		1983	Report on the Study of the Irritation to the Eye of the White Rabbit Based on Draize of 2,4-D. Study Number 83/0192. Unpublished
SA 94106		1994	2,4-D-Acute eye irritation test in the rabbit. Study number: SA 94106. GLP. Unpublished
00722B		1994	Acute Eye Irritation/Corrosion tests with Sanachem 2,4-D Acid Technical in rabbits. Study Number: 00722B. GLP. Unpublished
94/0516		1994	2,4-D: Delayed contact hypersensitivity study in the guinea-pig. Study number: 94/0516. GLP. Unpublished
2184-105		1986	Dermal Sensitization Study in Guinea Pigs: 2,4-Dichlorophenoxyacetic Acid. Study Number 2184-105. GLP. Unpublished.
00738C		1994	Contact hypersensitivity to Sanachem Simazine 500 SC in Albino Guinea Pigs (Magnusson Klingman Maximization Test. Study number:00738C. GLP. Commissioned by SANACHEM (PTY) LTD. Unpublished
1368600; R-90013957		2011	Local Lymph Node Assay (LLNA) In Mice. Study Number: 1368600. GLP. Unpublished
2184-116		1991	Subchronic Toxicity Study in Rats with 2,4-Dichlorophenoxyacetic Acid. Study Number 2184-116. GLP. Unpublished.
2184-117		1991	Subchronic Toxicity Study in Mice with 2,4-Dichlorophenoxyacetic Acid. Study Number 2184-117. GLP. Unpublished.
2184-115		1990	Subchronic Toxicity Study in Dogs with 2,4-Dichlorophenoxyacetic Acid. Study Number 2184-115. GLP. Unpublished.
2184-125		1993	13-Week Dietary Toxicity Study of 2,4-D in Dogs. Study Number 2184-125. GLP. Hazleton Washington, Inc., USA. Unpublished.
2184-106		1990	21-Day Dermal Irritation and Dermal Range-Finding Study in Rabbits with 2,4-Dichlorophenoxyacetic Acid. Study Number 2184-106. Unpublished.
2184-109		1990	21-Day Dermal Irritation and Dermal Toxicity Study in Rabbits with 2,4-Dichlorophenoxyacetic Acid. Study Number 2184-109. GLP. Unpublished.
07-6156		2008	A 28-Day Subchronic Inhalation Toxicity Study of 2,4-Dichlorophenoxyacetic Acid in the Rat via Nose-Only Exposures. Study Number 07-6156. GLP. Unpublished.
WIL-81135		1983	A Teratology Study in Fischer 344 Rats with 2,4-Dichlorophenoxyacetic Acid. Study Number WIL-81135. GLP. Unpublished.
320-003		1990	Developmental Toxicity (Embryo-Fetal Toxicity and Teratogenic Potential) Study of 2,4-Dichlorophenoxyacetica Acid (2,4-D Acid) Administered Orally via Stomach Tube to New Zealand White Rabbits. Study Number 320-003. GLP. Unpublished.
WIL-81137		1985	A Dietary Two-Generation Reproduction Study in Fischer 344 Rats with 2,4-Dichlorophenoxyacetic Acid. Study Number WIL-81137. GLP. Unpublished.

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
WIL-81137		1986	A Dietary Two-Generation Reproduction Study in Fischer 344 Rats with 2,4-Dichlorophenoxyacetic acid; Addendum to the Final Report. Study Number WIL-81137. GLP. Unpublished.
081104		2010	Summary: 2,4-D: An F1-Extended One Generation Dietary Toxicity Study in CRL:CD(SD) Rats. Study Number 081104. GLP. Unpublished.
081104		2010	2,4-D: An F1-Extended One Generation Dietary Toxicity Study in CRL:CD(SD) Rats. Study Number 081104. GLP. Unpublished.
K-002372-064F		1995	2,4-Dichlorophenoxyacetic Acid: Chronic Toxicity/Oncogenicity Study in Fischer 344 Rats – Final Report. Study Number K-002372-064F. GLP. Unpublished.
K-002372-064N		1994	2,4-Dichlorophenoxyacetic Acid: Chronic Neurotoxicity Study in Fischer 344 Rats. Study Number K-002372-064N. GLP. Unpublished.
2184-124		1993	52-Week Dietary Toxicity Study with 2,4-D in Dogs. Study Number 2184-124. GLP. Unpublished.
2184-101		1987	Oncogenicity Study in Mice with 2,4-Dichlorophenoxyacetic Acid (2,4-D). Study Number 2184-101. GLP. Unpublished.
K-002372-063F		1995	2,4-Dichlorophenoxyacetic Acid: Dietary Oncogenicity Study in B6C3F1 Mice (female) – Two Year Final Report. Study Number K-002372-063F. GLP. Unpublished.
K-002372-063M		1995	2,4-Dichlorophenoxyacetic Acid: Dietary Oncogenicity Study in Male B6C3F1 Mice – Two Year Final Report. Study Number K-002372-063M. GLP. Unpublished.
K-002372-066		1994	2,4-Dichlorophenoxyacetic Acid (2,4-D): Acute Neurotoxicity Study in Fischer 344 Rats. Study Number K-002372-066. GLP. Unpublished.
111121		2011	Evaluation of 2,4-Dichlorophenoxy Acetic Acid (2,4-D) in an in vitro Estrogen Receptor Binding Assay. Study Number 111121. GLP. Unpublished
111043		2011	Evaluation of 2,4-Dichlorophenoxy Acetic Acid (2,4-D) in an in vitro Estrogen Receptor Transcriptional Activation Assay in Human Cell Line HELA-9903. Study Number 111043. GLP. The Unpublished.
111111		2011	Evaluation of 2,4-Dichlorophenoxy Acetic Acid (2,4-D) in an in vitro Androgen Receptor Binding Assay. Study Number 111111. GLP. Unpublished.
111038		2011	Evaluation of 2,4-Dichlorophenoxy Acetic Acid (2,4-D) in the in vitro Steroidogenesis Assay. Study Number 111038. GLP. Unpublished.
111036		2011	2,4-Dichlorophenoxyacetic Acid: Evaluation of 2,4-Dichlorophenoxyacetic Acid in the Human Recombinant Aromatase Assay. Study Number 111036. GLP. Unpublished.
10979-0-401		1990	Mutagenicity Test on 2,4-Dichlorophenoxyacetic Acid (2,4-D) in the Salmonella/Mammalian-Microsome Reverse Mutation Assay (Ames Test). Study Number 10979-0-401. GLP. Unpublished.
10979-0-447		1990	Mutagenicity Test on 2,4-Dichlorophenoxyacetic Acid (2,4-D) in the In Vitro Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay. Study Number 10979-0-447. GLP. Hazleton Laboratories America, Inc., USA. Unpublished.
10979-0-455		1990	Mutagenicity Test on 2,4-Dichlorophenoxyacetic Acid In Vivo Mouse Micronucleus Assay. Study Number 10979-0-455. GLP. Unpublished.

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
24810		2009	Mutagenicity study of 2,4-D Acid in Salmonella typhimurium reverse mutation assay (in vitro). Study Number 24810. GLP. Germany. Unpublished.
24809		2009	Micronucleus Test of 2,4-D acid in bone marrow cells of the NMRI mouse by oral administration. Study Number 24809. Unpublished.
131053		2013	Evaluation of 2,4-Dichlorphenoxyacetic Acid In The Chinese Hamster Ovary Cell/Hypoxantine-Guianine-Phosphoribosyl Transferase (CHO/HGPRT) Forward Mutation Assay. Study number: 131053. GLP. Unpublished.
103-307		1990	(2,4-Dichlorophenoxyacetic Acid) 2,4-D: A Dietary LC50 Study with the Mallard. Study Number 103-307. GLP. Unpublished
G/17/03		2004	2,4-D ACID: Avian reproduction toxicity test in the Japanese Quail (Coturnix coturnix japonica). Study Number G/17/03. GLP. Unpublished
379-239		2011	2,4-Dichlorophenoxyacetic acid: An Acute Oral Toxicity Study with the Canary (Serinus canaria). Study Number 379-239.GLP. Unpublished
103-306		1990	(2,4-Dichlorophenoxyacetic Acid) 2,4-D: A Dietary LC50 Study with the Northern Bobwhite. Study Number 103-306. GLP. Unpublished
467-106		2000	2,4-D: A Reproduction Study with the Northern Bobwhite. Study Number 467-106. GLP. Unpublished
G/64/03		2004	KWAS 2,4-D: Acute Oral Toxicity Test with Japanese Quail (Coturnix coturnix japonica). Study Number G/64/03. GLP. Unpublished
467-118		2014	2,4-D Acid: A Dietary LC50 Study with the Canary. Study Number 467-118. GLP. Unpublished
ES-DR-0002-2297-4		1983	The Acute Toxicity if (2,4-Dichlorophenoxy) Acetic Acid to Representative Aquatic Organisms. Study Number ES-DR-0002-2297-4. GLP. Unpublished
W/56/03		2004	Common Carp – Acute toxicity Freshwater Fish. Study Number: W/56/03. GLP. Unpublished.
W/22/03		2003	2,4-D ACID: Daphnia magna acute immobilization test. Study Number W/22/03. GLP. Unpublished
3903008000-0200-3140		1990	2,4-Dichlorophenoxyacetic Acid: Acute Toxicity to Pink Shrimp (Penaeus duorarum) Under Flow-Through Conditions. Study Number 3903008000-0200-3140. GLP. Unpublished
ES-DR-0002-2297-10		1990	2,4-Dichlorophenoxyacetic Acid: Evaluation of the Toxicity to Early Life Stages of the Fathead Minnow, Pimephales promelas Rafinesque. Study Number ES-DR-0002-2297-10. GLP. Unpublished
W/24/03		2004	2,4-D ACID: Fish, juvenile growth test. Study number: W/24/03. GLP. Unpublished
W/25/03		2004	2,4-D ACID: Fish, early life stage. Study number: W/25/03. GLP. Unpublished
9040-D		1991	Chronic Toxicity of 2,4-D to the Daphnid, Daphnia magna. Study Number 9040-D. GLP. Unpublished
W/23/03		2003	2,4-D ACID: Daphnia magna reproduction test. Study number: W/23/03. GLP. Poland. Unpublished

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
467A-102		1997	2,4-D (2,4-Dichlorophenoxyacetic Acid): A 96-Hour Static Acute Toxicity Test with the Leopard Frog Tadpoles (Rama pipiens). Study Number 467A-102. GLP. Unpublished
101025		2010	2,4-Dichlorophenoxyacetic Acid: The Amphibian Metamorphosis Assay using the South African Clawed Frog, Xenopus laevis. Study Number 101025. GLP. Unpublished
101026		2010	2,4-Dichlorophenoxyacetic Acid: A Fish Short-term Reproduction Assay using the Fathead Minnow, Pimephales promelas. Study Number 101026. GLP. Unpublished
10-05-1		1997	Effect of 2,4-Dichlorophenoxyacetic acid on the Growth and Reproduction of Lemna gibba G3. Study Number 10-05-1. GLP. Carolina Ecotox, Inc., USA. Unpublished
W/57/03		2004	2,4-D ACID: Toxicity evaluation for duckweed Lemna minor L. UTCC 490. Study Number W/57/03. GLP. Unpublished
0460-05-1100-1		1990	The Toxicity of 2,4-D to Selenastrum capricornutum. Study Number 0460-05-1100-1. GLP. Unpublished.
10-01-1		1994	The Toxicity of 2,4-D to Anabaena flos-aquae. Study Number 10-01-1. GLP. Carolina Ecotox, Inc., USA. Unpublished
10-01-2		1994	The Toxicity of 2,4-D to Navicula pelliculosa. Study Number 10-01-2. GLP. Unpublished
10-01-3		1994	The Toxicity of 2,4-D to Skeletonema costatum. Study Number 10-01-3. GLP. Unpublished
379A-148A		2011	2,4-dichlorophenoxyacetic acid: A 72-hour toxicity test with the freshwater alga (Pseudokirchneriella subcapitata). Study Number 379A-148A. GLP. Unpublished
67558		2011	Rebstock, M. (2011), 2,4-D Acid: Growth Inhibition Test with the Freshwater Diatom, Navicula pelliculosa. Study Number: 67558. GLP. Unpublished
W/55/03		2004	2,4-D ACID: toxicity evaluation for algae. Study number: W/55/03. GLP. Unpublished
W/24/04		2005	2,4-D ACID: growth inhibition test for Anabaena flos-aquae. Study number: W/24/04.GLP. Unpublished
379A-150A		2011	2,4-Dichlorophenoxyacetic Acid: A 72-hour Toxicity Test with the Marine Diatom (Skeletonema costatum). Study Number 379A-150A. GLP. Unpublished
W/24/04		2005	2,4-D ACID: growth inhibition test for Skeletonema Costatum. Study Number W/24/04. GLP. Unpublished
64731031		2012	Study on the Effect of 2,4-D technical on Honey Bee Brood (*Apis mellifera* L.) – Brood Feeding Test. Study Number 64731031. GLP. IBACON. Germany. Unpublished
G/63/03		2004	2,4-D ACID, Earthworm reproduction test (Eisenia fetida Sav.). Study number: G/63/03. GLP. Institut of Organic Industry Branch Pszczyna. Poland. Unpublished
379E-102		2011	2,4-Dichlorophenoxyacetic acid: an activated sludge respiration inhibition test. Study number: 110234. GLP. Wildlife International, Ltd. Unpublished
286-DE		1993	2,4-D: Acute Flow-Through Mollusk Shell Deposition Test. Study Number 286-DE. GLP. T.R. Unpublished

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
3903008000-0210-3140		1990	2,4-Dichlorophenoxyacetic Acid: Acute Toxicity to Tidewater Silverside (Menidia Beryllina) Under Flow-Through Conditions. Study Number 3903008000-0210-3140. GLP. Unpublished

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
IPCS, 1984		1984	http://www.inchem.org/documents/ehc/ehc/ehc29.htm#PartNumber:9
IPCS, 1987		1987	http://www.inchem.org/documents/hsg/hsg/hsg005.htm
JMPR, 2001		2001	http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Reports_1991-2006/REPORT2001.pdf, p.43
JMPR, 2017		2017	http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Report2017/5.9_2_4-D__020_.pdfhttp://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Report2017/5.9_2_4-D__020_.pdf
EPA, 2005		2005	https://archive.epa.gov/pesticides/reregistration/web/pdf/24d_red.pdf
CIR, 2015		2015	https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2015.298.01.0008.01.ENG&toc=OJ:L:2015:298:TOC
HC, 2017		2017	https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/decisions-updates/reevaluation-note/2017/rev2017-08-re-evaluation-note-update-2-4-d.html
AGP: CP/100		1984	http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-old/en/
AGP:CP/310		1994	http://www.fao.org/agriculture/crops/core-themes/theme/pests/jmps/ps-old/en/
FAO/WHO Manual		2016	http://www.fao.org/3/a-i5713e.pdf
Margerison		2019	E-mail from Samuel Margerison, sent on 16 April 2019, 11:54:46 AM [From samuel.margerison@apvma.gov to laszlo.bura@efsa.europa.eu]
Karassali, 1		2019	E-mail from Καρασαλή Ελένη, sent on 16 April 2019, 11:54:46 AM [From: e.karassali@bpi.gr to laszlo.bura@efsa.europa.eu] (Dow)
Karassali, 2		2019	E-mail from Καρασαλή Ελένη, sent on 16 April 2019, 12:23:44 PM [From: e.karassali@bpi.gr to laszlo.bura@efsa.europa.eu] (Nufarm)
Bressant		2019	E-mail from Bressant Janet, sent on 25 April 2019, 11:58:34 AM [From: Bressant.Janet@epa.gov to laszlo.bura@efsa.europa.eu]
Kielek		2019	E-mail from Przemyslaw Kielek, sent on 13 July 2019 9:13 [From: przemyslaw.kielek@minrol.gov.pl to laszlo.bura@efsa.europa.eu]
JMPR, 1996		1996	http://www.inchem.org/documents/jmpr/jmpmono/v96pr04.htm

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
CIPAC, F	Martijn A and Dobrat W	1995	CIPAC Handbook Volume F. Physico-chemical Methods for Technical and Formulated Pesticides
CIPAC, J	Martijn A and Dobrat W	2000	CIPAC Handbook Volume J. Analysis of Technical and Formulated Pesticides
CIPAC, 1C	Henriet J, Martijn A and Povlsen H.H	1985	CIPAC Handbook Volume 1C. Analysis of Technical and Formulated Pesticides
KPN0134	Comb AL	2011	2,4-D pure Vapour pressure and Calculation of Volatility(Henry's Law Constant) Study KPN0134. Report KPN0134 GLP. Huntingdon Life Sciences Ltd, England. Unpublished
FAPC-G-10-66	Frank A	2011a	Determination of melting point and decomposition temperature of 2,4-D acid pure active ingredient. Study Number FAPC-G-10-66. GLP. Dow AgroSciences LLC. USA. Unpublished.
KPN0135	Comb AL	2011	2,4-D pure Water Solubility. Study KPN0135. Report KPN0135 GLP. Huntingdon Life Sciences Ltd, England. Unpublished
KPN0136	Comb AL	2011	2,4-D pure Partition Coefficient. Study KPN0136. Report KPN0136 GLP. Huntingdon Life Sciences Ltd, England. Unpublished
5135A	Cohen SP, Tamma RV and Creeger SM	1989	Hydrolysis of 2,4-D in aqueous solutions buffered at pH 5, 7, and 9. Study Number 5135A. GLP. Center for Hazardous Materials Research. Unpublished
1002382	Lewis CJ and Fletcher TA	2011c	[14C] 2,4-D: Photodegradation and Quantum Yield in Sterile pH 7 Buffer and Natural Water. Study number: 1002382. Covance Laboratoratories Limited. GLP, Unpublished
KPN0137	Comb AL	2011	2,4-D pure Dissociation Constant. Study KPN0137. Report KPN0137 GLP. Huntingdon Life Sciences Ltd, England. Unpublished
KPN0142	Comb AL	2011	2,4-D Technical Solvent Solubility. Study KPN0142. Report KPN0142 GLP. Huntingdon Life Sciences Ltd, England. Unpublished.
490-001	Johnson DE, Myer JR, Urain LC	1981	Determination of Acute Oral LD50 in Fischer 344 Rats (2,4-Dichlorophenoxyacetic acid, technical). Study Number 490-001. GLP. International Research and Development Corporation. USA. Unpublished.
SA 94109	Dange M.	1994	2,4-D-Acute Oral LD50 in the rat. Study number: SA 94109. GLP. Rhône Poulenc Secteur Agro. France. Unpublished
005961	Wandrag S.	1993	Oral and Dermal LD_{50} tests with Sanachem Sanaphen-D (2,4-D Acid Technical) in rats. Study Number: 005961. GLP. Roodeplaat Research Laboratories (Pty) Ltd. South Africa. Unpublished
005961	Wandrag S.	1993	Oral and Dermal LD_{50} tests with Sanachem Sanaphen-D (2,4-D Acid Technical) in rats. Study Number: 005961. GLP. Roodeplaat Research Laboratories (Pty) Ltd. South Africa. Unpublished
105837	Leonie A.L.	2011	Acute Oral Toxicity (Acute Toxic Class Method) with 2,4-D Acid. Study number: 105837. GLP. Bioservice Scientific Laboratories GmbH. Unpublished

Study number	Author(s)	Year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study.
490-004	Johnson D.E., Myer J.R., Marroquin F.	1981	2,4-Dichlorophenoxyacetic acid technical Determination of Acute Dermal LD50 in Fischer 344 Rats. Study number: 490-004. GLP. International Research and Development Corporation. USA. Unpublished
SA 94107	Dange M.	1994	2,4-D-Acute Dermal LD50 in the rat. Study number: SA 94107. GLP. Rhône Poulenc Secteur Agro. France. Unpublished
WIL-81233	Mayhew D	1981	Acute Dermal Toxicity Study in Albino Rabbits with ITF-5; 2,4-Dichlorophenoxyacetic Acid, Sodium Salt. Study Number WIL-81233. GLP. WIL Research Laboratories, Inc. USA. Unpublished
86-7893	Auletta CS and Daly IW	1986	An Acute Inhalation Toxicity Study of 2,4-Dichlorophenoxyacetic Acid in the Rat. Study Number 86-7893. GLP. Bio/dynamics Inc. USA. Unpublished.
83/0190	Kirsch P. and Hilderbrand, B.	1983	Report on the study of the irritation to the intact and abraded dorsal skin of the white rabbit based on Draize of 2,4-D. Study number: 83/0190. GLP. BASF AKTIENGESELLSCHAFT. Germany. Unpublished.
K-002372-060	Berdasco NM	1992	2,4-Dichlorophenoxyacetic Acid: Primary Dermal Irritation Study in New Zealand White Rabbits. Study Number K-002372-060. GLP. The Dow Chemical Company. USA. Unpublished.
SA 94104	Dange M.	1994	2,4-D-Acute dermal irritation test in the rabbit. Study number: SA 94104. GLP. Rhône Poulenc Secteur Agro. France. Unpublished
00735A.	Wandrag S.	1994	Acute dermal irritation and corrosion tests with Sanachem 2,4-D amine 480 g/L in rabbits. Study Number: 00735A. GLP. Biocon Research (Pty) Ltd. South Africa. Unpublished
83/0192	Kirsch P	1983	Report on the Study of the Irritation to the Eye of the White Rabbit Based on Draize of 2,4-D. Study Number 83/0192. BASF Aktiengesellschaft. Germany. Unpublished
SA 94106	Dange M.	1994	2,4-D-Acute eye irritation test in the rabbit. Study number: SA 94106. GLP. Rhône Poulenc Secteur Agro. France, Unpublished
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