

## 2,4-Dichlorophenoxyacetic acid (2,4-D); CASRN 94-75-7

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the [IRIS assessment development process](#). Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the [guidance documents located on the IRIS website](#).

STATUS OF DATA FOR 2,4-Dichlorophenoxyacetic acid (2,4-D)

**File First On-Line 03/31/1987**

Category (section)	Assessment Available?	Last Revised
<b>Oral RfD (I.A.)</b>	yes	03/31/1987
<b>Inhalation RfC (I.B.)</b>	not evaluated	
<b>Carcinogenicity Assessment (II.)</b>	not evaluated	

### I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

#### I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — 2,4-Dichlorophenoxyacetic acid (2,4-D)

CASRN — 94-75-7

Last Revised — 03/31/1987

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of

information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

NOTE: The Oral RfD for 2,4-D may change in the near future pending the outcome of a further review now being conducted by the Oral RfD Workgroup.

### I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
<b>Hematologic, hepatic and renal toxicity</b>	NOAEL: 1.0 mg/kg/day LOAEL: 5.0 mg/kg/day	100	1	1E-2 mg/kg/day
<b>90-Day Rat Oral Bioassay and 1-Year Interim Report from a 2-Year Rat Oral Bioassay</b>				
<b>Dow Chemical Co., 1983</b>				

\*Conversion Factors: none

### I.A.2. Principal and Supporting Studies (Oral RfD)

Dow Chemical Co. 1983. Acc. No. 251473. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Hematologic, hepatic, and renal toxicity were demonstrated in a study in Fischer rats (strain 344) during subchronic feeding performed at the Hazleton Laboratories (1983). 2,4-D (97.5% pure) was added to the diet chow and fed to the rats for 91 days at doses calculated to be 0.0 (controls), 1.0, 5.0, 15.0, or 45.0 mg/kg/day. In each of the five groups there were 20 animals/sex and 40 animals/treatment group, for a total of 200 animals. Criteria examined to determine toxicity were survival, daily examination for clinical symptomatology, weekly change in body weights, growth rates, food intake, ophthalmologic changes, changes in organ weights, and clinical, gross and histopathologic alterations. The results of the study demonstrated statistically significant

reductions in mean hemoglobin (both sexes), mean hematocrit and red blood cell levels (both sexes), and mean reticulocyte levels (males only) at the 5.0 mg/kg/day dose or higher after 7 weeks. There were also statistically significant reductions in liver enzymes LDH, SGOT, SGPT, and alkaline phosphatase at week 14 in animals treated at the 15.0 mg/kg/day or higher doses. Kidney weights (absolute and relative) showed statistically significant increases in all animals at the 15.0 mg/kg/day dose or higher at the end of the experimental protocol. Histopathologic examinations correlated well with kidney organ weight changes showing cortical and subcortical pathology. Increases in ovarian weights, T-4 levels, and a decrease in BUN were reported, but were not considered to be treatment- related.

In a second part of this study (Dow Chemical Co., 1983), B6C3F1 mice (20/sex/group) were fed the diet chow mixed with 97.5% pure 2,4-D at 0.0, 5.0, 15.0, 45.0 or 90.0 mg/kg bw/day (calculated doses) for 91 days. Criteria used to determine toxicity were the same as for rats. The only effect reported at 5 mg/kg/day was increased weight of adrenals in females. Effects at 15 mg/kg/day included altered organ weights and hematologic effects. Kidney weights were not affected below 45 mg/kg/day.

### **I.A.3. Uncertainty and Modifying Factors (Oral RfD)**

UF — The 100-fold uncertainty factor accounts for both interspecies and interhuman variability in the toxicity of this chemical in lieu of specific data. Because an analysis of the 90-day and 1-year interim results suggests that the NOAEL would hold for the full 2-year duration, inclusion of the subchronic-to-chronic UF is not warranted.

MF — None

### **I.A.4. Additional Studies/Comments (Oral RfD)**

The subchronic studies previously discussed provide a more sensitive basis for the RfD than available chronic or reproduction studies. Chronic toxicity and reproduction studies of 2,4-D indicated no adverse effects at dietary levels up to 500 ppm in dogs (approximately 14.5 mg/kg bw/day), up to 1250 ppm in rats (approximately 62.5 mg/kg bw/day) (Hansen et al., 1971), or at levels of 1000 ppm in drinking water (50-100 mg/kg bw/day) in pregnant rats (exposed through gestation and for 10 months following parturition) or their offspring (exposed for up to 2 years after weaning) (Bjorklund and Erne, 1966). A secondary reference to another study reported an increase in mortality among rats whose dams received approximately 50 mg/kg bw/day of 2,4-D in the diet for 3 months before mating and throughout gestation and lactation (Gaines and Kimbrough, 1970).

### **I.A.5. Confidence in the Oral RfD**

Study — Medium  
Database — Medium  
RfD — Medium

Confidence in the principal study is medium because a fair number of animals of each sex was used, four doses were given, and a good number of parameters were measured. Confidence in the database is medium because several studies support both the observation of critical toxic effects and the levels at which they occur. Medium confidence in the RfD follows.

#### **I.A.6. EPA Documentation and Review of the Oral RfD**

Source Document — U.S. EPA, 1984

This document has received several internal EPA reviews, reviews by outside expert scientists and a public review.

Other EPA Documentation — None

Agency Work Group Review — 05/20/1985, 02/05/1986

Verification Date — 02/05/1986

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for 2,4-Dichlorophenoxyacetic acid (2,4-D) conducted in November 2001 identified one or more significant new studies. IRIS users may request the references for those studies from the IRIS Hotline at [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) or (202)566-1676.

#### **I.A.7. EPA Contacts (Oral RfD)**

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) (internet address).

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#### **I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)**

Substance Name — 2,4-Dichlorophenoxyacetic acid (2,4-D)  
CASRN — 94-75-7

Not available at this time.

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## II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — 2,4-Dichlorophenoxyacetic acid (2,4-D)  
CASRN — 94-75-7

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

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III. [reserved]

IV. [reserved]

V. [reserved]

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## VI. Bibliography

Substance Name — 2,4-Dichlorophenoxyacetic acid (2,4-D)  
CASRN — 94-75-7

### VI.A. Oral RfD References

Bjorklund, N. and K. Erne. 1966. Toxicological studies of phenoxyacetic herbicides in animals. *Acta. Vet. Scand.* 7: 364-390.

Dow Chemical Company. 1983. Accession No. 251473. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Gaines, T. and R. Kimbrough. 1970. Personal Communication. (Cited in Hansen et al., 1971).

Hansen, W.H., M.L. Quaife, R.T. Habermann and O.G. Fitzhugh. 1971. Chronic toxicity of 2,4-dichlorophenoxyacetic acid in rats and dogs. *Toxicol. Appl. Pharmacol.* 20(1): 122-129.

U.S. EPA. 1984. Drinking Water Criteria Document for 2,4- Dichlorophenoxyacetic Acid (2,4-D). Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC.

### VI.B. Inhalation RfC References

None

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### VI.C. Carcinogenicity Assessment References

None

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### VII. Revision History

Substance Name — 2,4-Dichlorophenoxyacetic acid (2,4-D)

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Date	Section	Description
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.

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### VIII. Synonyms

Substance Name — 2,4-Dichlorophenoxyacetic acid (2,4-D)

CASRN — 94-75-7

Last Revised — 03/31/1987

- 94-75-7
- ACETIC ACID, (2,4-DICHLOROPHENOXY)-
- ACIDE 2,4-DICHLORO PHENOXYACETIQUE
- ACIDO(2,4-DICLORO-FENOSI)-ACETICO
- AGROTECT
- AMIDOX
- AMOXONE
- AQUA-KLEEN
- BH 2,4-D
- BRUSH-RHAP
- B-SELEKTONON
- CHLOROXONE

- CROP RIDER
- CROTILIN
- 2,4-D
- D 50
- DACAMINE
- 2,4-D ACID
- DEBROUSSAILLANT 600
- DECAMINE
- DED-WEED LV-69
- DESORMONE
- (2,4-DICHLOR-FENOXY)-AZIJNZUUR
- DICHLOROPHENOXYACETIC ACID
- 2,4-Dichlorophenoxyacetic acid
- Dichlorophenoxyacetic acid, 2,4-
- 2,4-DICHLORPHENOXYACETIC ACID
- (2,4-DICHLOR-PHENOXY)-ESSIGSAEURE
- DICOPUR
- DICOTOX
- DINOXOL
- DMA-4
- DORMONE
- 2,4-DWUCHLOROFENOKSYOCTOWY KWAS
- EMULSAMINE BK
- EMULSAMINE E-3
- ENT 8,538
- ENVERT 171
- ENVERT DT
- ESTERON
- ESTERONE FOUR
- ESTONE
- FARMCO
- FERNESTA
- FERNIMINE
- FERNOXONE
- FERXONE
- FOREDEX 75
- FORMULA 40
- HEDONAL
- HERBIDAL
- IPANER
- KROTILINE
- LAWN-KEEP
- MACRONDRAY
- MIRACLE
- MONOSAN

- MOXONE
- NA 2765
- NETAGRONE
- NETAGRONE 600
- NSC 423
- PENNAMINE
- PENNAMINE D
- PHENOX
- PIELIK
- PLANOTOX
- PLANTGARD
- RCRA WASTE NUMBER U240
- RHODIA
- SALVO
- SPRITZ-HORMIN/2,4-D
- SPRITZ-HORMIT/2,4-D
- TRANSAMINE
- TRIBUTON
- TRINOXOL
- U 46DP
- U-5043
- VERGEMASTER
- VIDON 638
- VISKO-RHAP
- WEED-AG-BAR
- WEEDAR-64
- WEEDATUL
- WEED-B-GON
- WEEDEZ WONDER BAR
- WEEDONE LV4
- WEED-RHAP
- WEED TOX
- WEEDTROL