

4,6-Dinitro-o-cyclohexyl phenol; CASRN 131-89-5

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 4,6-Dinitro-o-cyclohexyl phenol

File First On-Line 08/22/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	08/22/1988
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	not evaluated	

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — 4,6-Dinitro-o-cyclohexyl phenol

CASRN — 131-89-5

Last Revised — 08/22/1988

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.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Cataract formation	NOAEL: None	1000	1	2E-3 mg/kg/day
Adult Human Subchronic Oral Study	LOAEL: 2.0 mg/kg/day			
Horner, 1942				

*Conversion Factors -- none

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

Horner, W.D. 1942. Dinitrophenol and its relation to formation of cataract. Arch. Ophthalmol. 27:1097-1121.

2,4-dinitrophenol (2,4-DNP) and 4,6-dinitro-o-cresol (4,6-DNOC) have been used clinically as weight reduction aids. Oral administration of 2-5 mg/kg/day 2,4-DNP or 0.35-1.5 mg/kg/day 4,6-DNOC produced cataracts in 0.1-1.0% of treated patients. Although data regarding the cataractogenic effects of 4,6-dinitro-o-cyclohexylphenol (4,6-DOCP) in humans were not available, it is expected that 4,6-DOCP administration would also result in cataract formation, since it is structurally related to 2,4-DNP and 4,6-DNOC. Because Spencer et al. (1948) showed that the lipid solubility of 4,6-DOCP (1.84 g/100 g of oil) is more closely related to the solubility of 2,4-DNP (1.67 g/100 g of oil) than 4,6-DNOC (5.98 g/100 g of oil) and that 4,6-DOCP and 2,4-DNP were about equally toxic on a weight basis (mg/kg/day) to rats in a subchronic feeding study, it is appropriate to derive an RfD by analogy to 2,4-DNP.

The Ambient Water Quality Criteria Document considered the lower end of the therapeutic dose range for 2,4-DNP (2.0 mg/kg/day) as a LOAEL for oral exposure. Individual variability, rather than total dose or duration of treatment, was the major determining factor for cataract formation. Since doses below therapeutic levels were not studied, no NOEL or NOAEL was defined.

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

UF — 10 for conversion of a LOAEL to a NOAEL, 10 for sensitive human subgroups and 10 for the short exposure duration.

MF — None

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

Tainter et al. (1933) reported that skin rashes, loss of taste for sweets and salts and gastrointestinal upset accompanied repeated 2,4-DNP intake in humans. Dose levels were not specified. At therapeutic doses of 2,4-DNP, Horner (1942) found occasional cases of granulocytosis, bone marrow effects and neuritis after an average of 10 weeks.

Spencer et al. (1948) showed that 2,4-DNP, 4,6-DNOC and 4,6-DOCP had similar effects in rats, but that 4,6-DNOC was toxic at lower doses than either of the other two compounds. Rats received between 0 and 0.10% 4,6-DNOC or 4,6-DOCP, or 0 and 0.20% 2,4-DNP, in the diet for 6 months. For 4,6-DOCP, the dietary levels of 0, 0.02, 0.05 and 0.10% corresponded to daily intakes of 0, 5.4-20, 13.5-50 and 27-100 mg/kg for these groups, respectively, based on each rat's weight and food consumption. At the lower two dietary concentrations, growth rates were depressed 3-10%, relative to control rates. At 0.10%, the growth rate was depressed 10-15% below control rates, and slight cloudy swelling of the liver was observed. These changes were comparable to the effects seen in separate groups of rats given the same doses of 2,4-DNP. Spencer et al. (1948) found no cataracts in rats given dietary 2,4-DNP or 4,6-DOCP for 6 months. The subchronic dietary rat study by Spencer et al. (1948) is not useful for the RfD derivation because experimental animals are not adequate models for the induction of cataracts in humans by low-level oral exposure to dinitrophenols, and, therefore, an RfD based on the rat data may not be adequately protective for humans. There are no data on teratogenic effects of 4,6-DOCP.

I.A.5. Confidence in the Oral RfD

Study — Low

Database — Low

RfD — Low

Confidence in the study is low because the experimental results were for a different, albeit similar, chemical and a NOEL was not defined. Database confidence is low because related human studies suggest that more severely toxic effects can occasionally occur at low doses and

animal data are inadequate for assessment of risk. Moreover, there are no data on the teratogenicity of 4,6-DOCP. Confidence in the resulting RfD is low.

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

Source Document — U.S. EPA, 1980

Limited peer review and ECAO-CIN review, 1980.

Other EPA Documentation — None

Agency Work Group Review — 12/15/1987

Verification Date — 12/15/1987

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 4,6-Dinitro-o-cyclohexyl phenol conducted in August 2003 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at 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 (internet address).

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

Substance Name — 4,6-Dinitro-o-cyclohexyl phenol

CASRN — 131-89-5

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — 4,6-Dinitro-o-cyclohexyl phenol
CASRN — 131-89-5

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

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — 4,6-Dinitro-o-cyclohexyl phenol
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VI.A. Oral RfD References

Horner, W.D. 1942. Dinitrophenol and its relation to formation of cataract. *Arch. Ophthalmol.* 27: 1097-1121.

Spencer, H.C., V.K. Rowe, E.M. Adams and D.D. Irish. 1948. Toxicological studies on laboratory animals of certain alkyldinitrophenols used in agriculture. *J. Ind. Hyg.* 30: 10-25.

Tainter, M.L., A.B. Stockton and W.C. Cutting. 1933. Use of dinitrophenol in obesity and related conditions: Progress report. *J. Pharmacol. Exp. Therap.* 101: 1472.

U.S. EPA. 1980. Ambient Water Quality Criteria for Nitrophenols. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Water Regulations and Standards, Washington, DC. EPA 440/5-80-063. NTIS PB 81-117749.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — 4,6-Dinitro-o-cyclohexyl phenol
CASRN — 131-89-5

Date	Section	Description
08/22/1988	I.A.	Oral RfD summary on-line
10/28/2003	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — 4,6-Dinitro-o-cyclohexyl phenol
CASRN — 131-89-5
Last Revised — 08/22/1988

- 131-89-5
- 6-cicloesil-2,4-dinitr-fenolo
- 2-cyclohexyl-4,6-dinitrofenol
- 2-cyclohexyl-4,6-dinitrophenol
- 6-cyclohexyl-2,4-dinitrophenol
- dinex
- dinitrocyclohexylphenol
- 2,4-dinitro-6-cyclohexylphenol

- 4,6-Dinitro-o-cyclohexyl phenol
- Dinitro-o-cyclohexyl phenol, 4,6-
- dinitro-o-cyclohexylphenol
- DN
- DN 1
- DNOCHP
- Dowspray 17
- ENT 157
- NA 9026
- pedinex
- phenol, 2-cyclohexyl-4,6-dinitro-
- phenol, 6-cyclohexyl-2,4-dinitro-
- RCRA waste number P034
- SN 46