Sodium diethyldithiocarbamate; CASRN 148-18-5

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 <u>IRIS assessment</u> <u>development process</u>. 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 <u>guidance documents located</u> on the IRIS website.

STATUS OF DATA FOR Sodium diethyldithiocarbamate

File First On-Line 01/31/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	01/31/1987
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 — Sodium diethyldithiocarbamate CASRN — 148-18-5 Primary Synonym — Dithiocarb Last Revised — 01/31/1987

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.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Reduced body weight	NOEL: 30 mg/kg/day	1000	1	3E-2 mg/kg/day
Rat Subchronic Oral Study	LOAEL: 100 mg/kg/day			
Sunderman et al., 1967				
Reduced body weight and cataracts in	NOEL: none			
females	LOAEL: 1250 ppm diet (62.5 mg/kg/day)			
Chronic Rat Bioassay				
NCI, 1979				

*Conversion Factors: 1 ppm = 0.05 mg/kg/day (assumed rat food consumption)

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

Sunderman, F.W., O.E. Paynter and R.B. George. 1967. The effects of the protracted administration of the chelating agent, sodium diethyldithiocarbamate (dithiocarb). Am. J. Med. Sci. 254: 46-56.

NCI (National Cancer Institute). 1979. Bioassay of sodium diethyldithiocarbamate for possible carcinogeneicity. NCI Carcinogenesis Tech. Rep. Ser. No. 172. DHEW(NIH) 79-1728.

Albino rats (25/sex/group) were dosed p.o. with 0, 30, 100, or 300 mg dithiocarb/kg bw/day for 90 days (Sunderman et al., 1967). A dose-related decrease in weight gain was observed for all treatment groups, but was statistically significant only for the 100 and 300 mg/kg/day groups. Food consumption was not reported. Red blood cell counts were reduced, and related endpoints were affected for animals in the highest dose group. Histopathologic analysis showed evidence of mild kidney effects at 300 mg/kg/day. Beagle dogs (2/sex/group) were treated according to the same protocol (Sunderman et al., 1967). Effects were noted for the high-dose (300 mg/kg/ day) group only. These animals exhibited slight body weight loss, hematologic effects, and mortality (one animal died at day 70).

F344 rats (50/sex/group) were fed dithiocarb at 0, 1250, or 2500 ppm for 2 years. Reduced body weights were observed for females at both doses (about 10% less than controls) and males at the high dose only. A statistically significant increase in the incidence of cataracts was observed in the treated females, but not in males. The rats are assumed to have consumed 5% of body weight/day during the 2-year exposure of the NCI (1979) study.

Short-term administrations of slightly higher doses have been associated with central nervous system lesions in rabbits and neonatal lambs, with considerable mortality in the latter species. Dithiocarb has been reported to cause pancreatic damage in rabbits.

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

UF — The uncertainty factor of 1000 reflects 10 for both intraspecies and interspecies variability to the toxicity of this chemical in lieu of specific data, and 10 for extrapolation of a subchronic effect level to its chronic equivalent.

MF — None

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

None.

I.A.5. Confidence in the Oral RfD

Study — High Database — Medium RfD — Medium

The principal study was well designed and adequately reported; the two subchronic studies are mutually supportive, with similar effects observed. Support for chronic effects is lacking, and

hematologic endpoints were not examined in the NCI study. Confidence in the database can be considered to be medium to low because of the lack of adequate chronic and reproductive data. Confidence in the RfD can also be considered medium to low.

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

Source Document — U.S. EPA, 1984

The ADI in the Health and Environmental Effects Profile document has received an Agencywide review with the help of two external scientists.

Other EPA Documentation — None

Agency Work Group Review — 10/09/1985

Verification Date — 10/09/1985

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 Sodium diethyldithiocarbamate conducted in September 2002 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at <u>hotline.iris@epa.gov</u> 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 — Sodium diethyldithiocarbamate CASRN — 148-18-5 Primary Synonym — Dithiocarb

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Sodium diethyldithiocarbamate CASRN — 148-18-5 Primary Synonym — Dithiocarb

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 — Sodium diethyldithiocarbamate CASRN — 148-18-5 Primary Synonym — Dithiocarb

VI.A. Oral RfD References

NCI (National Cancer Institute). 1979. Bioassay of sodium diethyldithio- carbamate for possible carcinogenicity. NCI Carcinogenesis Tech. Rep. Ser. No. 172. DHEW(NIH) 79-1728.

Sunderman, F.W., O.E. Paynter and R.B. George. 1967. The effects of the protracted administration of the chelating agent, sodium diethyldithiocarba- mate (dithiocarb). Am. J. Med. Sci. 254: 46-56.

U.S. EPA. 1984. Health and Environmental Effects Profile for Sodium Diethyldithiocarbamate. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste, Washington, DC.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Sodium diethyldithiocarbamate CASRN — 148-18-5 Primary Synonym — Dithiocarb

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

VIII. Synonyms

Substance Name — Sodium diethyldithiocarbamate CASRN — 148-18-5 Primary Synonym — Dithiocarb Last Revised — 01/31/1987

- 148-18-5
- CARBAMIC ACID, DIETHYLDITHIO-, SODIUM SALT
- CARBAMODITHIOIC ACID, DIETHYL-, SODIUM SALT

- CUPRAL
- DDC
- DEDC
- DEDK
- DIETHYLCARBAMODITHIOIC ACID, SODIUM SALT
- DIETHYLDITHIOCARBAMATE SODIUM
- DIETHYLDITHIOCARBAMIC ACID, SODIUM SALT
- DIETHYL SODIUM DITHIOCARBAMATE
- Dithiocarb
- DITHIOCARBAMATE
- NCI CO2835
- SODIUM DEDT
- Sodium Diethyldithiocarbamate
- SODIUM N,N-DIETHYLDITHIOCARBAMATE
- SODIUM SALT of N,N-DIETHYLDITHIOCARBAMIC ACID
- THIOCARB
- USAF EK-2596