Cacodylic acid; CASRN 75-60-5

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 Cacodylic acid

File First On-Line 11/01/1992

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	11/01/1992

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Cacodylic acid
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Not available at this time.

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

Substance Name — Cacodylic acid
CASRN — 75-60-5

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Cacodylic acid
CASRN — 75-60-5
Last Revised — 11/01/1992

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

II.A. Evidence for Human Carcinogenicity

II.A.1. Weight-of-Evidence Characterization

Classification — D; not classifiable as to human carcinogenicity

Basis — No human data and inadequate data in animals.

II.A.2. Human Carcinogenicity Data

None.

II.A.3. Animal Carcinogenicity Data

Inadequate. In an 18-month study using B6C3F1 and B6AKF1 strain mice, groups of 18 mice/sex/strain were administered daily gavage doses of 46.4 mg/kg/day in distilled water (an amount determined in a previous test to be the maximum tolerated dose) from days 7-28 (NCI, 1968; Innes et al., 1969). At day 28, adjustments were made for body weight changes, and a concentration of 121 ppm cacodylic acid, which was calculated to deliver an equivalent daily dose, was added to the diet for the remainder of the 80-week test period. Survival at the end of the study in the B6C3F1 mice was 11/18 and 18/18 in the males and females, respectively, and was 17/18 and 16/18 in the B6AKF1 males and females, respectively. No significant differences in tumor incidence were reported when treated groups were compared with those of untreated and pooled untreated controls. The tumor incidences in the control and pooled control groups could not be determined from the reports. The incidences of reticulum cell sarcoma in treated male B6C3F1 and treated B6AKF1 female mice were 2/14 and 2/18, respectively. The total tumor incidences among treated groups were 3/14, 0/18, 1/18 and 4/18 in male and female B6C3F1 mice and in male and female B6AKF1 mice, respectively.

In a second NCI (1968) study, which also used mice strains B6C3F1 and B6AKF1, a single subcutaneous injection of cacodylic acid at 464 mg/kg in distilled water was administered in the nape of the neck to 18 28-day weanlings/sex/strain to screen for carcinogenicity. Survival at the end of the study was 10/18, 18/18, 14/18 and 15/18 in the treated B6C3F1 male and female mice and in the B6AKF1 male and female mice, respectively. Tumor incidences reportedly were not significantly increased over controls. Tumor incidences in the control and pooled control groups could not be determined from the reports. Tumor incidences among the treated groups were 4/18, 2/18, 3/18 and 3/18 in the male and female B6C3F1 mice and in the male and female B6AKF1 mice, respectively.

II.A.4. Supporting Data for Carcinogenicity

Johansen et al. (1984) studied the promoting effect of cacodylic acid on liver tumors induced in male Wistar rats by diethylnitrosamine (DENA). Partially hepatectomized rats (26) were injected intraperitoneally with saline (controls) or 30 mg/kg of DENA. On postsurgery day 7, 80 ppm (MTD) cacodylic acid was administered in drinking water to both groups. The investigators estimated an average dose of approximately 3.8 mg/rat/day. Body weight was monitored weekly, and rats were sacrificed and necropsied after 6 months. Histopathological examinations were limited to the liver and kidney. Renal tumors developed in 2/11 rats receiving only DENA and in 3/7 rats receiving both compounds (this increase was not statistically significant); saline injection followed by cacodylic acid treatment alone produced no tumors (0/8). The average number of tumors in the DENA group was 0.36 (s.d. 0.24) and in the group receiving DENA and cacodylic acid it was 0.71 (s.d. 0.26). The increased incidence of liver lesions, basophilic foci, and

neoplastic nodules occurring among rats receiving both DENA and cacodylic acid was not statistically significant, when compared to the group that received only DENA. The authors concluded that these results suggest a tumor promoting effect of cacodylic acid despite the lack of statistical significance, which might have been shown if an increased number of animals had been studied and/or if the dose of DENA had been reduced.

Cacodylic acid has been tested for mutagenicity and genotoxicity in bacteria, yeast, Drosophila, and mammalian cell cultures with positive and negative results. In reverse mutation assays using Escherichia coli and Salmonella typhimurium strains, cacodylic acid was negative in either the presence or absence of S9 (Simmon et al., 1977; Jones et al., 1984; Andersen et al., 1972). The results of DNA repair assays in S. typhimurium were negative (Jones et al., 1984) and in Bacillus subtilus and E. coli were inconclusive (Simmon et al., 1977; Jones et al., 1984); these assays were performed both with and without S9. In mitotic recombination and mitotic crossing over assays using Saccharomyces cerevisiae, cacodylic acid was positive both with and without S9 (Jones et al., 1984; Simmon et al., 1977; Riccio et al., 1981). Tests for nondisjunction and loss of sex chromosomes in Drosophila were negative (Ramel and Magnusson, 1979) as was the sex-linked recessive lethal test (Valencia, 1981).

Results from mammalian cell tests were both positive and negative. In both a sister chromatid exchange assay in Chinese hamster ovary (CHO) cells (Jones et al., 1984) and a reverse mutation (comutagenicity) assay also in CHO cells (Taylor et al., 1984) cacodylic acid tested negative. In a forward mutation assay using mouse lymphoma L5178Y TK+/- cells, cacodylic acid tested positive in the presence of S9 (Jones et al., 1984) but was negative in an unscheduled DNA synthesis assay in human fetal lung fibroblast cells (WI-38 cells) (Simmon et al., 1977). A bone marrow micronucleus test (Jones et al., 1984) was positive at the highest dose tested (750 mg/kg initially and 1500 mg/kg 1 day later) when mice were administered cacodylic acid.

II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

None.

II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

None.

II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)

II.D.1. EPA Documentation

Source Document — U.S. EPA, 1989

The 1989 Health and Environmental Effects Document for Cacodylic Acid has received full review from the Office of Health and Environmetal Assessment and from the Office of Pesticides and Toxic Substances.

II.D.2. EPA Review (Carcinogenicity Assessment)

Agency Work Group Review — 09/05/1991

Verification Date — 09/05/1991

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer assessment for Cacodylic acid conducted in September 2002 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 or (202)566-1676.

II.D.3. EPA Contacts (Carcinogenicity Assessment)

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).

VI. Bibliography

Substance Name — Cacodylic acid
CASRN — 75-60-5

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

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Valencia, R. 1981. Mutagenesis screening of pesticides in "Drosophila." EPA-600/1-81-017. NTIS Publ. No. PB81-160848. 71 p.

VII. Revision History

Substance Name — Cacodylic acid
CASRN — 75-60-5

Date	Section	Description
11/01/1992	II.	Carcinogenicity assessment on-line
12/03/2002	II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Cacodylic acid
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- 75-60-5
- ACIDE CACODYLIQUE [FRENCH]
- ACIDE DIMETHYLARSINIQUE [FRENCH]
- ACIDO CACODILICO [SPANISH]
- AGENT BLUE
- ANSAR
- ANSAR 138
- ARSAN
- ARSINE OXIDE, HYDROXYDIMETHYL-

- ARSINIC ACID, DIMETHYL-
- ARSINIC ACID, DIMETHYL-
- CACODYLIC ACID
- CASWELL NO. 133
- CHEXMATE
- DILIC
- DIMETHYLARSENIC ACID
- DIMETHYLARSINIC ACID
- DIMETHYLARSINIC ACID
- EPA PESTICIDE CHEMICAL CODE 012501
- ERASE
- HSDB 360
- HYDRODIMETHYLARSINE OXIDE
- HYDROXYDIMETHYLARSINE OXIDE
- KYSELINA KAKODYLOVA [CZECH]
- NSC 103115
- PHYTAR
- PHYTAR 138
- PHYTAR 560
- RAD-E-CATE 35
- RCRA WASTE NUMBER U136
- SILVISAR
- SILVISAR 510
- SYLVICOR
- UN 1572