1-Chlorobutane; CASRN 109-69-3

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 1-Chlorobutane

File First On-Line 04/01/1990

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	04/01/1990*

*A comprehensive review of toxicological studies was completed (07/22/05) - please see section II.D.2. for more information.

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — 1-Chlorobutane
CASRN — 109-69-3

Not available at this time.

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

Substance Name — 1-Chlorobutane
CASRN — 109-69-3

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — 1-Chlorobutane
CASRN — 109-69-3
Last Revised — 04/01/1990

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 — Based on no human carcinogenicity data and inadequate animal data.

II.A.2. Human Carcinogenicity Data

None.

II.A.3. Animal Carcinogenicity Data

Inadequate. The National Toxicology Program (NTP, 1986) conducted a 2- year toxicology and carcinogenesis study of 1-chlorobutane in male and female B6C3F1 mice and F-344/N rats. Groups of 50 animals/sex/species were gavaged with 1-chlorobutane (99.5% pure) in corn oil at 0, 500, or 1000 mg/kg/day (mice) or 0, 60, or 120 mg/kg/day (rats), 5 days/week for 103 weeks. Because of high mortality, all mice dosed at 1000 mg/kg/day were sacrificed in the 45th week and a second study with additional groups of 50 mice/sex was started at 0 and 250 mg/kg/day.

In the mouse studies, survival (54-64%) was comparable for vehicle controls and 500-mg/kg/day groups in the first study, and also for vehicle controls and 250-mg/kg/day groups in the second study (50-72%) (NTP, 1986). Only the 1000-mg/kg/day male mice showed lower mean body weights compared with vehicle controls after week 36. An increased incidence of alveolar/ bronchiolar adenomas or carcinomas (combined) (as evaluated by the Incidental Tumor Test) was observed in females in the 500 mg/kg group (9/50) compared with its vehicle controls (3/50), and no effect was seen in the 250 mg/kg group (8/50 treated vs. 6/50 vehicle control). The incidences of these tumors were not statistically significantly elevated (Incidental Tumor Test) when treated groups were compared with pooled vehicle control groups (9/100) from the first and second part of the study. In addition, the lack of hyperplasia in females and the negative trend seen in males suggest that these marginal effects were not treatment-related.

A statistically significant increased incidence of hepatocellular adenomas or carcinomas (combined) was observed in females in the 500 mg/kg group (8/50 vs. 3/50) but not in the 250 mg/kg group (9/50 vs. 7/50) when compared by Incidental Tumor Tests. When compared by Incidental Tumor Tests with pooled vehicle controls from the two studies, however, the incidence was not statistically significantly elevated. In the first study, there was an increased incidence (not statistically significant) of hemangiosarcomas in males (1/50, control; 3/50, low-dose; 4/50, high-dose), but such an increase was not observed in males in the second study (4/50 control vs. 2/50 at 250 mg/kg); nor when treated animals were compared with pooled vehicle controls. Since the incidences of hepatocellular adenomas and carcinomas in females were highly variable between the vehicle controls in the two studies (2-16%) and there were no dose-related effects in male mice, these tumors in female mice were not considered treatment-related. The hemangiosarcomas in male mice were also not considered to be compound-related, as the incidence in the vehicle controls was highly variable (2-8%) and the incidence in the first study was lower than the NTP historical incidence which is 4%.

In the rat study (NTP, 1986), survival was significantly reduced in high- dose males (17/50 treated vs. 50/50 vehicle control) and females (11/50 vs. 35/50); however, the authors felt survival throughout the study was adequate for proper analysis of the carcinogenic potential of 1-chlorobutane. Mean body weight of treated and control rats were comparable throughout the

study. Pheochromocytomas of the adrenal gland were significantly increased in the low-dose females (1/50, vehicle control; 6/50, low-dose; and 1/49, high-dose). The incidence of medullary hyperplasia, an expected preneoplastic observation associated with these tumors (observed in 3/50 vehicle controls; 7/50 low-dose females; and 4/49 high-dose females) did not suggest a neoplastic phenomenon in progress. The incidence of pheochromocytomas was low, not dose-related, and not seen in male rats. Furthermore, pheochromocytomas are late-developing tumors and they were not considered to be treatment related. Thus, NTP concluded that there was no evidence of carcinogenicity of 1-chlorobutane for male and female mice or male and female rats under the conditions of these studies. It was noted, however, that the chemical-induced mortality in high- dose rats suggest toxic levels were reached and reduce the sensitivity of the study for determining carcinogenicity.

Poirier et al. (1975) gave groups of 10 male and 10 female strain A/Heston mice a total of 24 i.p. injections (3 injections/week) of 12.9, 32.4, or 65 mmol/kg (1194, 3000, or 6017 mg/kg) 1-chlorobutane in tricaprylin. Untreated and tricaprylin-treated mice were used as negative controls, and urethane- treated mice were used as positive controls. Mice were sacrificed 24 weeks after the first injection. Survival at termination of the study was >90%. No statistically significant increase in the average number of lung tumors per mouse occurred in mice given 1-chlorobutane. This assay scores only lung tumors and is considered to be a short-term in vivo screening test.

II.A.4. Supporting Data for Carcinogenicity

When tested in the Salmonella/microsomal assay, 1-chlorobutane was nonmutagenic in strains TA98, TA100, TA1535, and TA1537 with and without the addition of hepatic homogenates (Eder et al., 1980, 1982a,b; Barber et al., 1981; Barber and Donish, 1982; Zeiger, 1987; Zeiger et al., 1987; NTP, 1986). In contrast, Simmon (1981) reported positive results in strain TA100 in the absence of hepatic homogenates; however, no control data were provided. Negative results were obtained in a chromosomal aberration test in rat bone marrow cells (Rudnev et al., 1979) and in a DNA damage assay in Escherichia coli (Fluck et al., 1976). 1-Chlorobutane was mutagenic in mouse lymphoma L5178Y assay in the absence of Aroclor-induced male rat liver S9 and was not tested in the presence of rat liver S9 (NTP, 1986). Negative results were obtained in chromosomal aberration tests and sister chromatid exchanges in Chinese hamster ovary cells with and without Aroclor-induced Sprague-Dawley rat liver S9 (NTP, 1986).

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, 1988

The 1988 Health and Environmental Effects Document for Monochlorobutanes has received Agencey review.

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

Agency Work Group Review — 09/07/1989

Verification Date — 09/07/1989

A comprehensive review of toxicological studies published through July 2005 was conducted. No new health effects data were identified that would be directly useful in the revision of the existing carcinogenicity assessment for 1-Chlorobutane and a change in the assessment is not warranted at this time. For more information, IRIS users may contact 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).

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — 1-Chlorobutane
CASRN — 109-69-3

VI.A. Oral RfD References

None

VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

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VII. Revision History

Substance Name — 1-Chlorobutane
CASRN — 109-69-3

Date	Section	Description
04/01/1990	II.	Carcinogen assessment on-line
12/03/2002	II.D.2.	Screening-Level Literature Review Findings message has been added.
08/15/2005	II.D.2.	Screening-Level Literature Review Findings message has been removed and replaced by comprehensive literature review conclusions.

VIII. Synonyms

Substance Name — 1-Chlorobutane
CASRN — 109-69-3
Last Revised — 04/01/1990

- 109-69-3
- Butane, 1-chloro-
- AI3-15309
- Butyl chloride
- CHLORURE DE BUTYLE [French]
- HSDB 4167
- n-BUTYL CHLORIDE
- n-PROPYLCARBINYL CHLORIDE
- NCI-C06155
- 1-chlorobutane