1,2-Dibromo-3-chloropropane (DBCP); CASRN 96-12-8

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 DBCP

File First On-Line 10/01/1991

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	yes	10/01/1991
Carcinogenicity Assessment (II.)	not evaluated	

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — 1,2-Dibromo-3-chloropropane (DBCP)
CASRN — 96-12-8

Not available at this time.

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

Substance Name — 1,2-Dibromo-3-chloropropane (DBCP)
CASRN — 96-12-8
Last Revised — 10/01/1991

The inhalation Reference Concentration (RfC) is analogous to the oral RfD and is likewise based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. The inhalation RfC considers toxic effects for both the respiratory system (portal-of-entry) and for effects peripheral to the respiratory system (extrarespiratory effects). It is expressed in units of mg/cu.m. In general, the RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Inhalation RfCs were derived according to the Interim Methods for Development of Inhalation Reference Doses (EPA/600/8-88/066F August 1989) and subsequently, according to Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry (EPA/600/8-90/066F October 1994). RfCs can also be derived for the noncarcinogenic health effects of substances that are 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.B.1. Inhalation RfC Summary

Critical Effect	Exposures*	UF	MF	RfC
Testicular effects **13-Week Subchronic Rabbit Inhalation Study** **Rao et al., 1982**	NOAEL: 0.94 mg/cu.m (0.1 ppm) NOAEL(ADJ): 0.17 mg/cu.m NOAEL(HEC): 0.17 mg/cu.m LOAEL: 9.4 mg/cu.m (1 ppm) LOAEL(ADJ): 1.7 mg/cu.m LOAEL(HEC): 1.7 mg/cu.m	1000	1	2E-4 mg/cu.m

*Conversion Factors: MW = 236.3. Assuming 25C and 760 mmHg, NOAEL (mg/cu.m) = 0.1 ppm x 236.3/24.45 = 0.97; adjusted for compound purity of 0.973 = 0.94 mg/cu.m. NOAEL(ADJ) = NOAEL (mg/cu.m) x 6 hours/24 hours x 5 days/7 days = 0.17 mg/cu.m. The NOAEL(HEC) was calculated for a gas:extrarespiratory effect in rabbits assuming periodicity

was attained. Since b:a lambda values are unknown for the experimental species (a) and humans (h), a default value of 1.0 is used for this ratio. NOAEL(HEC) = 0.17 mg/cu.m.

I.B.2. Principal and Supporting Studies (Inhalation RfC)

Rao, K.S., J.D. Burek, F. Murray, et al. 1982. Toxicologic and reproductive effects of inhaled 1,2-dibromo-3-chloropropane in male rabbits. Fund. Appl. Toxicol. 2(5): 241-251.

Rao et al. (1982) exposed 6-month-old male New Zealand white rabbits (10/group) to 0, 0.1, 1 or 10 ppm (0, 0.94, 9.4 or 94 mg/cu.m) DBCP vapors (adjusted for 97.3% purity), 6 hours/day, 5 days/week (duration-adjusted to 0, 0.17, 1.7, and 17 mg/cu.m), for 14 weeks. The rabbits receiving the 10-ppm concentration were exposed for only 8 weeks due to high mortality (apparently from pneumonia). Body weights and hematological and clinical chemistry parameters were monitored, but no significant differences were found between the DBCP-exposed animals and the controls. Semen was collected and evaluated during the exposure and during a 32 to 38 week recovery period to assess sperm motility, viability, and count. The average sperm count of the rabbits exposed to the 10-ppm concentration was significantly less than that of the controls after 7 weeks of exposure, and remained decreased for the duration of the exposure period and through week 42 of postexposure. At 1 ppm DBCP, sperm counts were significantly reduced compared with controls from weeks 11 to 13 of exposure. At 0.1 ppm, sperm counts were sporadically lower than control values although this was statistically significant only once, during exposure week 12. The percentage of live sperm in the semen of the rabbits exposed to 10 ppm DBCP was also significantly decreased compared with control values during weeks 8 to 26. Rabbits exposed to 1 ppm DBCP, but not those exposed to 0.1 ppm, exhibited significant decreases in the percentage of live sperm during weeks 6, 12 and 13. From the 8th week of exposure onward, the rabbits exposed to 10 ppm DBCP had a marked decrease in the percentage of progressively motile sperm. No consistent statistically significant decreases in this parameter were noted in the two lower exposure groups. Abnormal spermatozoa within the seminiferous tubules of 3 to 4 rabbits from each exposure group were counted; the percentage of abnormal sperm at 14 weeks was 5% for controls, 10% for animals exposed to 0.1 ppm DBCP and 18% for animals exposed to 1 ppm DBCP.

To assess the effects of DBCP on fertility, exposed male rabbits were mated to unexposed female rabbits at weeks 14 and 41 of the study. DBCP did not affect the libido of the exposed male rabbits during week 14 based on the percentage of males (78-100%) that copulated with unexposed females. However, the five males exposed to 10 ppm DBCP were infertile since none of the females became pregnant. The mean number of implantations/litter in the 1 ppm group was significantly less than that of the control group. During week 41 (27 weeks post-exposure), all rabbits exposed to 0.1 and 1 ppm DBCP produced normal litters, and 2 of the 5 males exposed to 10 ppm regained fertility (i.e., increased sperm count) and produced normal litters.

The follicle stimulating hormone (FSH) serum levels were also significantly elevated at 14 weeks in the males exposed to 1 ppm DBCP and at 46 weeks in the males exposed to 10 ppm DBCP. Increased FSH serum levels were consistent with a marked decrease in sperm count, whereas serum levels of testosterone were unchanged. The only gross lesion observed under macroscopic examination was the small size of the testes for rabbits exposed to 1 and 10 ppm DBCP. No gross lesions were observed in either the lungs or upper respiratory tract, and micropathology was not performed. Other histopathologic examination revealed changes in the reproductive system. These effects included atrophy of the testes, epididymides, and accessory sex glands including the prostate. The testes weight was significantly decreased to 50% of control values (week 14) in the group exposed to 1 ppm and to 75% of control values (week 8) in the group exposed to 10 ppm. Severe testicular atrophy was characterized by nearly complete or complete loss of spermatogenic elements in nearly all seminiferous tubules. Following the recovery period, tubular regeneration was observed in testes of some rabbits exposed to 10 ppm DBCP; 3 of 5 rabbits had regeneration such that 25% of the seminiferous tubules appeared normal. At the 1 ppm exposure, recovery was nearly complete in some rabbits although no incidences were given. Testes of rabbits exposed to 0.1 ppm DBCP appeared normal. Thus, rabbits exposed to 0.1 ppm DBCP showed no major treatment- related changes, and this level is designated as a no effect level. The NOAEL(HEC) is 0.17 mg/cu.m and the LOAEL(HEC) is 1.7 mg/cu.m. The respiratory tracts were not histologically examined in this study.

I.B.3. Uncertainty and Modifying Factors (Inhalation RfC)

UF — An uncertainty factor of 10 is used for the protection of sensitive human subpopulations. A factor of 3 is used for interspecies extrapolation, as the concentration was dosimetrically adjusted to humans. A full factor of 10 is applied for the use of a subchronic study to reflect the marginal NOAEL in the principal study, as the minor testicular effects seen at the NOAEL were consistent with the effects seen at the higher LOAEL in this and other investigations. A study of chronic duration could result in these minor effects progressing into more delineated adverse effects. A factor of 3 is used for database deficiency because of the lack of a multigenerational reproductive study, and inhalation development toxicity studies. The total uncertainty factor is therefore 1000.

MF — None

I.B.4. Additional Studies/Comments (Inhalation RfC)

Whereas a number of occupational studies on exposure to DBCP demonstrate this compound to be a potent testicular toxicant in humans, none of these occupational studies to date have evaluated the possible respiratory tract effects of DBCP exposure. This is especially disturbing when the inhalation studies conducted by NTP (1982) established the efficacy of this compound

to produce lesions and tumors in the nasal cavity of both rats and mice; Sax (1989) lists this compound as both an eye and skin irritant. Little reliable exposure data are available from any of these studies. Also, most are confounded as they have been conducted in pesticide manufacturing plants where workers are co-exposed to a number of other chemicals. Limited followup studies of effected worker populations indicate that paternal exposure to DBCP sufficient to produce oligospermia or azoospermia did not detectably increase the rate of congenital malformations or impair the health status of offspring conceived during or after DBCP exposure. DBCP is, however, a potential mutagen capable of inducing a dominant lethal effect in mice (Teramoto et al., 1980).

A cross-sectional study of 23 male workers at a DBCP production facility showed a 79% incidence (18 of 23) of azoospermia and oligospermia (Potashnik et al., 1979). No estimates of DBCP concentrations were given although exposure hours were presented. The exposure hours reported for a subgroup of 12 of these men diagnosed as azoospermic (sperm count = 0) ranged from 100 to 6726 hours. For another subgroup of six men diagnosed as oligospermic (designated as less than 10 million sperm/mL) the reported exposure hours ranged from 34 to 95 hours. The remaining 5 men had normal sperm counts and exposure hours ranging from 10 to 60. The azoospermic men had elevated FSH, but normal LH and testosterone levels. Testicular biopsy showed atrophy of seminiferous epithelium and tubules lined by Sertoli cells. In a 4-year followup study on 17 of these effected workers (plus three others not in the original study group), sperm count recovered in 4 of the 13 initially azoospermic men and 5 of the 7 oligospermic men (Potashnik, 1983). There was no improvement in the sperm count of the remaining 11 men who had prolonged exposure to DBCP. In another followup study (8-year) on 15 of the same group of effected workers, perinatal outcome as measured by birth defects, prematurity, mortality, or spontaneous abortions was not associated with paternal exposure to DBCP (Potashnik and Yanai-Inbar, 1987). In another subgroup of 11 of these effected workers, the rate of birth or health defects in their families following exposure was not different from that of a group of children from the same families conceived during the pre-exposure period (Potashnik and Phillip, 1988). In contrast, Kharrazi et al. (1980) report a statistically significant increase in the percentage of spontaneous abortions in wives of men working in Israeli banana plantations and in direct contact with DBCP. Levels of DBCP exposure were not given although the extent of exposure ranged from 1 season to 20 consecutive seasons. Sperm levels were not measured in this study, and there may have been selection bias among the participants as only 62 of 102 possible participants were interviewed for the study.

In a limited cross-sectional study, 11 of 25 men working in a DBCP- formulating plant were found to be azoospermic or oligospermic (designated as less than 1 million sperm/mL ejaculate) and had elevated serum levels of FSH and LH (Whorton et al., 1977). The average exposure of the 11 men with a very low sperm count was 8 years. DBCP levels were purported to have been measured early in 1977 with personal air-sampling devices and indicated an 8 hour average

concentration of 0.4 ppm (3.9 mg/cu.m), although no further specifics were available. Testicular biopsy, performed in 10 of these 25 men by Biava et al. (1978) showed that the diminution of spermatogenesis was correlated with duration of exposure to DBCP. Men with 10-year exposures had ejaculate without sperm and seminiferous tubules devoid of germ cells. Exposure for 1 to 3 years produced marked diminution of sperm formation and spermatogenic activity limited to a few segments of the tubules. Spermatogenic activity in men exposed for less than a year was classified as normal. A followup study in a subgroup of these same workers conducted 7 years after the initial evaluation showed that 2 of 8 workers that were originally classified as azoospermic produced some sperm during the followup, although only one had normal sperm production (Eaton et al., 1986). These results suggest that damage to germinal tissue by DBCP exposure sufficient to produce sterility is permanent. Although the exposure is poorly characterized, 3.9 mg/cu.m DBCP appears to be a frank-effect-level (FEL) in humans based on cases of azoospermia.

Laboratory animal studies via other routes confirm the testicular, respiratory, and adrenal effects of DBCP. Studies with other species indicate the rabbit to be the most sensitive test species for testicular effects (Pease et al., 1991). The drinking water studies of Foote et al. (1986a,b) in rabbits were carefully and thoroughly executed to elucidate several aspects of DBCP on male reproductive function. In the 1986a study, dose-related decreases in the proportion of abnormal sperm as well as a biochemical indicator of impaired spermatogenesis (elevated FSH levels) were documented. The 1986b study demonstrated dose-related quantitative testicular histology including effects on testicular weight, alterations in seminiferous tubular diameter and a marked decrease of all germ cell types.

Sprague-Dawley rats (30/sex/group) were exposed to 0, 0.1, 1 or 10 ppm (0, 0.97, 9.7, or 97 mg/cu.m) DBCP vapor, 6 hours/day, 5 days/week (duration adjusted to 0, 0.17, 1.7 or 17 mg/cu.m), for 14 weeks, followed by a 32-week recovery period (Rao et al., 1983) for a total of 46 weeks. Body weight and clinical examinations were made throughout the study. At the 14-week sacrifice, absolute and relative testes and epididymides weights were significantly decreased compared with controls only in the group exposed to 10 ppm DBCP. At the 46-week sacrifice, only the relative testes weight in the males exposed to 10 ppm was significantly lower than controls. No significant differences were seen in organ weights of exposed female rats compared with their controls. There were no treatment-related gross lesions observed in animals after 4 weeks of exposure. At the 14-week sacrifice, histopathological changes occurred in testes (decreased size and dark color; decreased spermatogenesis in individual seminiferous tubules, lack of germinal cells in 5/5 males) and in the adrenal gland (foci of altered cells in cortex in 3/5 males and 3/5 females) of the animals exposed to 10 ppm DBCP. At the 46-week terminal sacrifice, testicular atrophy was observed in a concentration-related manner in all male groups (12/18 at 10 ppm, 5/20 at 1 ppm, 3/19 at 0.1 ppm) including controls (2/17). Adrenal cortical hyperplasia was noted in both sexes at the 10 ppm concentration (32/35) and in the females at the

terminal kill at the 1 ppm concentration (7/19). Ovarian cysts were observed in females at the terminal sacrifice at the highest concentration (7/17). Another concentration-related effect observed only in the female animals at terminal (46 week) sacrifice was cortical hematocyst formation in 1 of 20 animals exposed to 0.1 ppm, in 4 of 19 animals exposed to 1 ppm, and in 16 of 17 animals exposed to 10 ppm. Mineralized deposits occurred in the cerebrum of the brain of both sexes (15/18 males and 6/17 females) in the high exposure animals at the terminal sacrifice. Although significance was not reported, DBCP markedly effected the animals exposed to 10 ppm and slightly effected the testes and the adrenals of the animals exposed to 1 ppm. Therefore, a mild LOAEL of 1 ppm DBCP (HEC = 1.73 mg/cu.m), based on testicular and adrenal effects, was determined from this subchronic study. The respiratory tract was not examined histopathologically in this study.

To assess fertility in male rats in this study (Rao et al., 1983), 20 males per exposure group were mated with unexposed females during weeks 2, 4, 6, 10, 12, 14, 16, 20, 24, 28, and 42. The percentage of males that impregnated at least one female was at least 85% for all the groups; no difference was seen between exposed and control males. In the group exposed to 10 ppm DBCP, a statistically significant increase ($p<0.05$) in post- implantation loss was observed during the fourth week of exposure and remained high through the remainder of the exposure period; this finding appears to be a treatment-related dominant lethal effect. By the tenth week of recovery, the average number of resorptions in the 10-ppm group was similar to that of the controls. No anomalies were observed in fetuses sired by exposed males during week 41 of the study. To assess fertility in exposed female rats, 20 exposed females per group were mated with unexposed males for a 5-day period during weeks 14, 18 and 20. Fertility of the exposed female rats was not significantly different from that of the controls except for a higher incidence of 10-ppm dams having litters of 4 or fewer pups. There were no significant differences between control and exposure groups and no major gross alterations in the pups.

The inhalation carcinogenesis bioassay conducted by NTP (1982) comprises four different studies involving rats and mice. These studies establish DBCP as a carcinogen, with high incidences of tumors appearing in the nasal cavity and on the tongues of rats and in the nasal cavity and lungs of mice. Focal hyperplasia in the nasal cavity was apparent in both species at the lower of the two exposure concentrations but may have been obscured by tumors at the higher concentration. Hyperplasia lower in the respiratory tract was also observed but at a less frequent incidence. Progression of these lesions, either into the lower respiratory tract or onto cancer, is implied but not proven by these observations. Consequently, HECs for respiratory effects in these studies are given for both extrathoracic (ET) and total pulmonary (TOT) surface areas. Though several HECs for effects in the ET area are as low as the proposed NOAEL(HEC), the RfC is based on testicular effects because of the human correlate and the confounding of nasal cavity lesions with cancerous lesions in the same anatomical area.

In a chronic carcinogenesis bioassay, F344 rats (50/sex/group) were exposed to 0, 0.6 or 3 ppm (0, 5.8 or 29 mg/cu.m) DBCP vapors, 6 hours/day, 5 days/week (duration adjusted to 0, 1.04 or 5.2 mg/cu.m). Results from this study are reported both in NTP (1982) and in Reznik et al. (1980b). The low- exposed rats were exposed for 103 weeks, and the high-exposed rats were exposed for 84 weeks due to excessive mortality. Body weights and clinical signs were recorded. Gross and microscopic examinations were performed on all major tissues including the testes and the nasal cavity where step cuts were made from the nostril to the cranium (the number of sections was not specified). A concentration-related respiratory effect observed in the male rats was focal hyperplasia of the nasal cavity in low-exposed and high-exposed (31/50 and 1/49) animals, respectively, that was not accompanied by an increased incidence in hyperplasia in either the bronchioles or the alveolar epithelium. In the female rats, the incidences of nasal cavity abscesses in the low- and high-exposed animals was 5/50 and 12/50, respectively, and 1/50 in the controls. Focal hyperplasia of the nasal cavity was noted in 24/50 of the low-exposure animals and in 23/50 of the high-exposure animals. This nasal cavity hyperplasia was not accompanied by increased incidences of hyperplasia in either the bronchioles or the alveolar epithelium. It should be noted that the decrease in focal hyperplasia of the nasal cavity of both male and female rats at the highest exposure level was concomitant with an increase in neoplastic lesions at this exposure. The nasal cavity of the high-exposed females also showed chronic inflammation (6/50), hyperkeratosis (11/50), and squamous metaplasia (15/50). Other systemic effects in the high- exposed female rats include hyperkeratosis of the esophagus (22/49), stomach hyperkeratosis (15/48) and acanthosis (12/48), toxic nephropathy (46/49), and necrosis of cerebrum (8/49). Pigmentation of the spleen occurred in 10/50, 28/50, and 34/48 female rats in the 0-, 0.6- and 3-ppm DBCP groups, respectively. Degeneration of adrenal cortex occurred in 19/50 and 13/48 of low- and high-exposed females compared with 4/50 in the controls. The incidence of pathology of the testes was inversely related to the concentration, hyperplasia of interstitial cells occurring in 41/50 controls and in 18/50 of low- and 6/48 high-exposed animals. Likewise, testicular degeneration occurred in 8/50 low-exposed animals, but only in 4/48 high-exposed animals. Other systemic effects in the high-exposed males were splenic pigmentation (13/49) and atrophy (8/49), hyperkeratosis of esophagus (18/49), and toxic nephropathy (49/49). A LOAEL of 0.6 ppm was identified based on the splenic, and adrenal gland effects; LOAEL(HEC) = 1.04 mg/cu.m. The concentration of 0.6 ppm is also designated as a LOAEL for respiratory effects; for the total pulmonary area, LOAEL(HEC) = 2.3 mg/cu.m and for the extrathoracic area, LOAEL:(HEC) = 0.19 mg/cu.m.

B6C3F1 mice (50/sex/group) were exposed to 0, 0.6, and 3 ppm (0, 5.8 and 29 mg/cu.m) DBCP vapors, 6 hours/day, 5 days/week (duration adjusted to 0, 1.04 and 5.2 mg/cu.m). Results from this study are reported both in NTP (1982) and in Reznik et al. (1980a). The low-exposed female mice were exposed for 103 weeks and the low-exposed male mice and high-exposed animals were exposed for only 76 weeks due to excessive mortality. Body weights and clinical signs were recorded. Gross and microscopic examinations were performed on all major tissues

including the testes and the nasal cavity where step cuts were made from the nostril to the cranium (number of sections not specified). Mean body weight gain was depressed by 17-28% in the high-exposed males after week 60 and by 25% in high-exposed females after week 76. The mortality in high-exposed females was significantly higher ($p<0.001$) than that of the other groups; 43 of 50 died during weeks 51 through 74, while mortality in the high-exposed males was comparable with other groups. Concentration- dependent respiratory effects observed in the male mice were focal hyperplasia of the nasal cavity in low-exposed and high-exposed (2/42 and 12/48) animals, respectively, as well as focal hyperplasia in the bronchioles (7/40 and 29/45) and hyperplasia of the alveolar epithelium (2/40 and 7/45). None of these effects were noted in any control animal. The high-exposed males also had a high incidence of suppurative inflammation in the nasal cavity (21/48) and focal hyperplasia of bronchi (14/45). Splenic atrophy (16/45), toxic nephropathy (9/46), and leukocytosis of lungs (4/45) were also evident in high-exposed males. There was also a high incidence of hyperkeratosis (10/41 and 17/44) and acanthosis (6/41 and 11/44) in the stomach, kidney inflammation (9/42 and 7/46), and necrosis of prepuce (7/42 and 3/48) in the 0.6 and 3 ppm groups compared with very low or no incidences in the controls. No concentration-dependent effects were noted in the testes, seminal vesicles, or epididymides. In the female mice, the incidences in the low- and high-exposed animals of suppurative inflammation was 5/50 and 13/50; of focal hyperplasia of the nasal cavity, 17/50 and 3/50; of hyperplasia of bronchioles, 5/49 and 11/47; of hyperplasia of alveolar epithelium, 5/49 and 11/47. It should be noted that the decrease in focal hyperplasia of the nasal cavity of both male and female mice at the highest exposure level was concomitant with an increase in neoplastic lesions at this exposure. A greater incidence of splenic atrophy (19/43) and endometrium cyst (11/45) occurred in the high-exposed animals. A high incidence of hyperkeratosis (20/48 and 24/46) and acanthosis (12/48 and 18/46) of the stomach was evident in both exposure groups. A LOAEL of 0.6 ppm DBCP, due to gastrointestinal and kidney effects (HEC = 1.04 mg/cu.m) was determined for this chronic study. The concentration of 0.6 ppm is also designated a LOAEL for respiratory effects; for the total pulmonary area, LOAEL(HEC) = 6.7 mg/cu.m and for the extrathoracic area, LOAEL(HEC) = 0.19 mg/cu.m.

In the rat subchronic study (NTP, 1982; also reported in Reznik et al., 1980c), Fischer 344 rats (5/sex/group) inhaled 0 (filtered room air), 1, 5 or 25 ppm (0, 9.66, 48.3 or 241.6 mg/cu.m) DBCP (96% purity), 6 hours/day, 5 days/week (duration adjusted to 1.7, 8.6 or 43 mg/cu.m), for 13 weeks. Both sexes of rats in the highest group exhibited blood stains around the nasal orifice throughout the 13-week period. Two females died during weeks 10 and 11 of exposure while two females and one male were sacrificed during weeks 10, 11, and 12 due to moribund conditions. There was a 60% decrease in body weight compared with controls, and severe hair loss in the rats exposed to 25 ppm DBCP. The high exposure animals also had inflammation and severe necrosis of the respiratory and olfactory epithelium in the dorsal part of the nasal cavity. The incidence of these lesions is reported to be concentration- related and is reported in the narrative section of the report only. Necrosis of the tracheal epithelium was found in 7 of the 10 rats

exposed to 25 ppm DBCP. In the lung, squamous metaplasia of the bronchial epithelium was present along with hyperplasia and partial regeneration of the bronchial and bronchiolar epithelium (data not presented). Atrophy with hypospermatogenesis was revealed in the testes of five male rats exposed to 25 ppm DBCP. With 1 and 5 ppm exposure levels, focal hepatic necrosis, hepatocytic hydropic changes, cytomegaly, and toxic tubular nephrosis were reported. A LOAEL of 1 ppm DBCP (HEC = 1.73 mg/cu.m) for liver and kidney alterations was determined. A LOAEL of 1 ppm is assumed for respiratory effects; for the total pulmonary area, LOAEL(HEC) = 2.23 mg/cu.m and for the extrathoracic area, LOAEL(HEC) = 0.19 mg/cu.m.

In the subchronic study in mice (NTP,1982; also reported in Reznik et al., 1980c) B6C3F1 mice (10/sex/group) were exposed to 0, 1, 5 or 25 ppm (9.66, 48.3 or 241.6 mg/cu.m) DBCP, 6 hours/day, 5 days/week (duration adjusted to 1.7, 8.6 or 43 mg/cu.m), for 13 weeks. Four of the males exposed to 25 ppm DBCP died before the end of the exposure period. Weight loss was 69% in males and 19% in females of the high-exposed group. Hydropic changes of the hepatocytes and nephrosis in the male mice exposed to 25 ppm and necrosis of the bronchiolar epithelium in the animals exposed to 25 ppm were reported. Regeneration and hyperplasia of the bronchiolar epithelium and megalocytic epithelial cells were found in all mice exposed to 5 ppm. Lesions in the epithelium of the nasal cavity (i.e., inflammation, necrosis, proliferative lesions) were also observed in mice exposed to 25 ppm DBCP. No data are presented for these effects; they are described in the narrative section of the report. Occurrence of lesions in other organs (e.g., testes, kidneys, or liver) are not discussed. A systemic NOAEL(HEC) for weight loss would be HEC = 1.73 mg/cu.m. A NOAEL of 1 ppm was assumed for respiratory effects; for the total pulmonary area, NOAEL(HEC) = 7.5 mg/cu.m and for the extrathoracic area, LOAEL(HEC) = 0.21 mg/cu.m.

Torkelson et al. (1961) conducted a series of inhalation exposures with DBCP in several species. In single exposures to rats at concentrations of 60 ppm (580 mg/cu.m) and higher, ocular and respiratory irritation was apparent. In preliminary range-finding studies, the authors reported mortality in rats subjected to a total of 15 7-hour exposures to 386 mg/cu.m (13/15 rats died), 48 such exposures to 193 mg/cu.m (10/15 died), and 50 such exposures at 97 mg/cu.m (2/15 died). Animals in the latter exposure group were described as having dulling of the corneas; weight loss; and hair loss, as well as gross lesions in the lungs, intestinal mucosa, kidneys, and testes. In a more extensive experiment, rats (20/sex), guinea pigs (10/sex), rabbits (3/sex), and monkeys (2 females) inhaled 12 ppm DBCP (116 mg/cu.m), 7 hours/day, 5 days/week, for a period of 70 to 92 days. Mortality was 40 to 50% in rats, and was attributed to lung infections. Much of the text is concerned with alterations in the genitalia, with severe atrophy and degeneration of the testes described in all species. Effects in rats included degenerative changes in the seminiferous tubules, increased Sertoli cells, reduced sperm count, and abnormal sperm. The respiratory tract was apparently not examined.

Although no inhalation developmental studies were located for this compound, Ruddick and Newsome (1979) performed a developmental study in which Wistar rats were gavaged with DBCP in corn oil. Pregnant rats (15/group) were randomized into four groups and gavaged doses of either 0 (vehicle), 12.5, 25, or 50 mg/kg of 97.5% DBCP on days 6 through 15 of gestation. Necropsies were carried out on day 22. DBCP was not teratogenic. No skeletal or visceral anomalies of significance were observed above those noted for control fetuses (data not shown). Mean fetal weights were significantly decreased in the highest dose group. Maternal weight gain was significantly decreased in the two highest dosed groups. The dose of 12.5 mg/kg was considered a NOAEL for maternal effects and 25 mg/kg was considered a NOAEL for fetal effects.

I.B.5. Confidence in the Inhalation RfC

Study — Medium
Database — Medium
RfC — Medium

The subchronic inhalation study in rabbits of Rao et al (1982) is given a medium confidence rating due to the lack of reporting respiratory effects. The database is given medium confidence. Although chronic studies in 2 different species exist, the available reproductive studies were limited and there is uncertainty about occurrence of respiratory tract effects relative to testicular effects. A medium confidence in the RfC follows.

I.B.6. EPA Documentation and Review of the Inhalation RfC

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — U.S. EPA, 1988

Agency Work Group Review — 08/15/1991

Verification Date — 08/15/1991

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfC for 1,2-Dibromo-3-chloropropane (DBCP) 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.B.7. EPA Contacts (Inhalation RfC)

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).

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — 1,2-Dibromo-3-chloropropane (DBCP)
CASRN — 96-12-8

Not available at this time.

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

VI. Bibliography

Substance Name — 1,2-Dibromo-3-chloropropane (DBCP)
CASRN — 96-12-8

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

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VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — 1,2-Dibromo-3-chloropropane (DBCP)
CASRN — 96-12-8

Date	Section	Description
10/01/1991	I.B.	Inhalation RfC now on-line
10/28/2003	I.B.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — 1,2-Dibromo-3-chloropropane (DBCP)
CASRN — 96-12-8
Last Revised — 10/01/1991

- 96-12-8
- Propane, 1,2-dibromo-3-chloro-
- Dibromochloropropane
- 1,2-dibromo-3-chloropropane
- AI3-18445
- BBC 12
- Caswell No. 287
- CCRIS 215
- DBCP
- Dibromchlorpropan [German]
- Dibromochloropropane
- EPA Pesticide Chemical Code 011301
- Fumagon
- Fumazone
- Fumazone 86E
- HSDB 1629
- NCI-C00500
- Nemabrom

- Nemafume
- Nemagon
- NEMAGON SOIL FUMIGANT
- Nemagon 20
- Nemagon 20G
- Nemagon 206
- Nemagon 90
- Nemanax
- Nemanex
- Nemapaz
- Nemaset
- Nemazon
- OS 1897
- OXY DBCP
- PROPANE, 1-CHLORO-2,3-DIBROMO-
- RCRA WASTE NUMBER U066
- SD 1897
- 1-CHLORO-2,3-DIBROMOPROPANE
- 1,2-DIBROM-3-CHLOR-PROPAN [German]
- 1,2-DIBROMO-3-CHLOROPROPANE
- 1,2-DIBROMO-3-CLORO-PROPANO [Italian]
- 1,2-DIBROOM-3-CHLOORPROPAAN [Dutch]
- 3-CHLORO-1,2-DIBROMOPROPANE