# Proposition 65 Maximum Allowable Dose Level (MADL) for Reproductive Toxicity for 1,2-Dibromo-3-chloropropane (DBCP)

## June 2004


## Office of Environmental Health Hazard Assessment (OEHHA)
## Reproductive and Cancer Hazard Assessment Section


## Summary


The maximum allowable dose level (MADL) for 1,2-dibromo-3-chloropropane (DBCP) is **4.3 micrograms/day (µg/day)** by the inhalation route of exposure and **3.1 µg/day** by the oral route of exposure. These MADLs were derived based on the male reproductive effects observed in rabbits by Rao et al. (1982).


## Background

This report describes the derivation of a maximum allowable dose level (MADL) for 1,2-dibromo-3-chloropropane (DBCP) (CAS No. 96-12-8).

DBCP was used as a soil fumigant and nematocide, but is no longer manufactured commercially or used agriculturally in the U.S. However, extensive use of DBCP in the past has resulted in contamination of soil and underground aquifers in several areas of this country, in particular the Sacramento Valley of California (OEHHA, 1999). DBCP was listed under Proposition 65 (the Safe Drinking Water and Toxic Enforcement Act of 1986) as known to the State to cause reproductive toxicity (male reproductive toxicity), effective February 27, 1987. The Proposition 65 listing of DBCP was based on the statutory requirement that "such list shall include at a minimum those substances identified in Labor Code Section 6382(b)(1) and those substances identified additionally by reference in Labor Code Section 6382(d)" (Health and Safety Code section 25249.8(a)). Labor Code Section 6382(d) requires that "any substance within the scope of the federal Hazard Communication Standard (29 C.F.R. Sec. 1910.1200) is a hazardous substance subject to this chapter." DBCP is recognized as a "Toxic and Hazardous Substance" by 29 C.F.R. Part 1910, Subpart Z and cited as an example for "reproductive toxins" in 29 C.F.R. Section 1910.1200, Appendix A (Health Hazard Definitions (29 C.F.R. Section 1910.1200) Appendix A (7)).

Procedures for the development of Proposition 65 MADLs are provided in regulations (Title 22, California Code of Regulations, §12801 and 12803). Exposure at a level 1,000 times greater than the MADL is expected to have no observable effect. As defined in regulations, a MADL is derived from a No Observable Effect Level (NOEL) based on the most sensitive study deemed to be of sufficient quality (Title 22 Cal. Code of Regs. §12803).

## Study Selection

Relevant studies on the male reproductive toxicity of DBCP have been identified through literature searches. These studies, listed in the Bibliography for this document, have been reviewed and considered for the establishment of the MADL.

The male reproductive toxicity of DBCP has been clearly shown in numerous epidemiological studies in humans. However, exposure data in human studies are not adequate for a dose-response assessment and thus they cannot be used for identification of a NOEL.

The male reproductive toxicity of DBCP has also been extensively studied in laboratory animals. Major findings from several relevant animal studies that provided lowest observable effect levels (LOELs) and/or NOELs by inhalation or oral route of exposure are briefly summarized in Table 1. No reproductive study following dermal exposure that is of sufficient quality for the purpose of MADL development was found in the literature.

The NOEL is based on the most sensitive study deemed to be of sufficient quality (Title 22 Cal. Code of Regs. §12803 (a)(4)). Based on the findings from studies listed in the Table 1 and the discussions presented above, OEHHA determined that the rabbit study by Rao et al. (1982), is the most sensitive study of sufficient quality and consequently this study was used for establishment of the MADL for DBCP.

In the study by Rao et al. (1982), male New Zealand white rabbits six months of age (ten animals per group) were exposed by inhalation to 0, 0.1, 1.0 or 10.0 ppm of DBCP, six hours/day, and five days per week for a total of 14 weeks. The body weights of the animals were not reported. DBCP used in the study was 97.3% pure. In animals exposed to $\geq$ 1 ppm of DBCP, the authors found decreased testicular weights, apparent testicular atrophy, decreased sperm counts in semen ejaculates, and reduced mean number of implantations. Thus, the LOEL and NOEL for DBCP in this study are 1.0 and 0.1 ppm, respectively (Rao et al., 1982). These exposure levels are equivalent to 0.61 and 0.061 mg/kg-day, respectively, based on the calculations presented below.

**Table 1. Summary of the Male Reproductive Toxicity of DBCP**

| Study Reference | Animals | Treatment | General Toxicity | Reproductive Effects & LOEL | NOEL (adjusted) |
|---|---|---|---|---|---|
| Rao et al., 1982 | Male New Zealand White rabbits, 10/group | **Inhalation**, 0, 0.1, 1.0, 10 ppm, 6 h/d, 5 d/wk for 14 wks | High mortality at 10 ppm; No other sign of general toxicity. | Decreased testis weights and sperm counts; testicular atrophy; increased serum FSH. LOEL=1.0 ppm (0.61 mg/kg-day) | 0.1 ppm (0.061 mg/kg-day) |
| Rao et al., 1983 | Sprague-Dawley rats, male, total of 30 rats per group. | **Inhalation,** 0, 0.1, 1.0, 10 ppm. 6 h/d, 5 d/wk for 14 weeks | No overt clinical sign of toxicity or change in body weight gain. | Decreased testis weights; testicular atrophy; increased post-implantation loss. LOEL= 1.0 ppm (0.95 mg/kg-day) | 0.1 ppm (0.10 mg/kg-day) |
| Foote et al., 1986a; 1986b | Dutch rabbits, male, 6/group | **Drinking water**, 0, 0.94, 1.88, 3.75, 7.5, 15 mg/kg, 5 d/wk, 10wks | No effect on body weight gain. No obvious general toxicity. | Decreased testis weights, epididymal sperm counts, and germ cell numbers. LOEL= 1.88 mg/kg | 0.94 mg/kg (0.64 mg/kg-day) |
| Heindel et al., 1989 | Sprague-Dawley rats, male, 20/group | **Drinking water**, 0, 5, 50, 100, 200 ppm for 64 days | Decreased body weight gain and water consumption. | Decreased testis weights; no effect on testicular morphology. LOEL= 200 ppm. | 100 ppm (5.4 mg/kg-day) |
| Amann & Berndtson, 1986 | Sprague-Dawley rats, male, 15/group | **Gavage**, 0, 0.94, 1.88, 3.75, 7.5, 15 mg/kg/d for 77 days | Decreased body weight gain at 15 mg/kg/d. | Decreased testis weights & sperm counts. LOEL= 15 mg/kg-day | 7.5 mg/kg-day |
| Ahmad et al., 1988 | Long-Evans rats, male, 6-30 per group | **Gavage**, 1,5, 25 mg/kg/d for up to six months. | Decreased body weights at 5 and 25. | Decreased testis weights; germ cell death. LOEL= 5 mg/kg-day | 1 mg/kg-day |
| Johnston et al., 1986 | Sprague-Dawley rats, one-generation reproduction study | **Drinking water**, 0, 0.02, 0.2, 2.0, 20 mg/kg/d; males and females were exposed. | Decreased body weight gains at 20 mg/kg-day. | Decreased average litter weight of pups at the highest dose; no effect on testis weights or morphology. | 20 mg/kg-day (14.47 mg/kg-day estimated by the authors) |
| Chapin & Sloane, 1997 | CD-1 mice, two-generation reproduc-tion study | **Gavage**, 0, 25, 50, 100 mg/kg, both males and females in two generations were exposed | No effect in body weight gains; increased relative liver weight in F1 male adults at 100 mg/kg | Decreased relative epididymis and prostate weights in F1 male adults at 100 mg/kg. LOEL =100 mg/kg-day | 50 mg/kg-day |

**Notes:** 1. Adjusted NOEL: NOELs reported in the original reports were adjusted to mg/kg-day following the methods described in the "MADL Calculation" section of this document.
2. Inhalation rate (IR) for rabbits was derived from body weights (W): IR ($m^3$/day) = 0.46*$W^{0.8307}$; U.S. EPA, 1988). For rats, the method by Anderson et al. was used: IR ($m^3$/day) = 0.105 $[W/0.113]^{2/3}$, (Anderson et al., 1983).

## MADL Calculation

The NOEL is the highest dose level which results in no observable reproductive effect, expressed in milligrams of chemical per kilogram of bodyweight per day. The NOEL is converted to a milligram per day dose level by multiplying the assumed human body weight by the NOEL ((Title 22 Cal. Code of Regs. §12803). For male reproductive toxicity, the assumed body weight of a man is 70 kg.

The following calculations were performed to derive the MADL for DBCP via inhalation, based on a NOEL of 0.1 ppm found in the rabbit study by Rao et al. (1982):

Conversion of air concentration in ppm to $mg/m^3$ using a conversion factor of 9.67 (OEHHA, 1999):

$0.1 \text{ ppm} \times 9.67 = 0.97 \text{ mg/m}^3$

Adjusting for purity (97.3%):

$0.97 \text{ mg/m}^3 \times 97.3\% = 0.94 \text{ mg/m}^3$

Calculation of NOEL expressed as mg/kg-day, based on a body weight of 3.73 kg for six-month-old male New Zealand white rabbits with an inhalation rate of 0.057 $m^3$/hr (see footnote 2 to Table 1):

$(0.94 \text{ mg/m}^3 \times 0.057 \text{ m}^3\text{/hr} \times 6 \text{ hr/day}) \div (3.73 \text{ kg}) = 0.086 \text{ mg/kg-day}$

Conversion from five days/week to seven days/week:

$0.086 \text{ mg/kg-day} \times (5 \text{ days} \div 7 \text{ days}) = 0.061 \text{ mg/kg-day}$

Calculation of NOEL for a 70 kg man:

$0.061 \text{ mg/kg-day} \times 70 \text{ kg} = 4.27 \text{ mg/day}$

The MADL is derived by dividing the NOEL by one thousand ((Title 22, Cal. Code of Regs., § 12801(b)(1)). Thus, the adjusted NOEL was divided by 1,000 to obtain the MADL.

$\mathbf{MADL_{inhalation}} = 4.27 \text{ mg/day} \div 1000 = 4.27 \text{ µg/day}$, or **4.3 µg/day** after rounding.

This MADL represents intake by the inhalation route of exposure. Approximately 50% of an administered dose of DBCP is absorbed via the inhalation route of exposure (Gingell et al., 1987; OEHHA, 1999). The MADL for DBCP via the inhalation route of exposure as proposed above is thus equivalent to an absorbed dose of approximately 2.2 µg/day ($4.3 \text{ µg/day} \times 50\%$).

In addition to the inhalation route of exposure, exposure of humans to DBCP can also occur via oral, dermal, or multiple routes of exposure. Approximately 70% (68-78%) of DBCP is absorbed in rats following oral administration (OEHHA, 1999). The absorbed

dose of 2.2 µg/day is thus equivalent to an intake of 3.1 µg/day following oral route of exposure (2.2 µg/day ÷ 70% = 3.1 µg/day). For the purposes of Proposition 65, the MADL for DBCP via the oral route of exposure is 3.1 µg/day.

If exposures occur by dermal or multiple routes, the total exposure to the chemical from a single source or product must be considered. The absorbed dose resulting from any one or multiple routes of exposure should be calculated. If the total absorbed dose resulting from any one or multiple routes is less than or equal to 2.2 µg/day, the MADL has not been exceeded.

## References


Anderson E, Carcinogen Assessment Group of the U.S. Environmental Protection Agency (1983). Quantitative approaches in use to assess cancer risk. *Risk Anal* **3**, 277-95.

Ahmad N, Wisner JR Jr, Warren DW (1988). Morphological and biochemical changes in the adult male rat reproductive system following long-term treatment with 1,2-dibromo-3-chloropropane. *Anat Rec* **222**, 340-9.

Amann RP, Berndtson WE (1986). Assessment of procedures for screening agents for effects on male reproduction: effects of dibromochloropropane (DBCP) on the rat. *Fundam Appl Toxicol* **7**, 244-55.

Chapin, RE, Sloane, RA (1997). Reproductive toxicology. Dibromochloropropane. *Environ Health Perspect* **105 Suppl 1**, 299-300.

Foote RH, Berndtson WE, Rounsaville TR (1986a). Use of quantitative testicular histology to assess the effect of dibromochloropropane (DBCP) on reproduction in rabbits. *Fundam Appl Toxicol* **6**, 638-47.

Foote RH, Schermerhorn EC, Simkin ME (1986b). Measurement of semen quality, fertility, and reproductive hormones to assess dibromochloropropane (DBCP) effects in live rabbits. *Fundam Appl Toxicol* **6**, 628-37.

Gingell R, Beatty PW, Mitschke HR, Page AC, Sawin VL, Putcha L, Kramer WG (1987). Toxicokinetics of 1,2-dibromo-3-chloropropane (DBCP) in the rat. *Toxicol Appl Pharmacol* **91**, 386-94.

Heindel JJ, Berkowitz AS, Kyle G, Luthra R, Bruckner JV (1989). Assessment in rats of the gonadotoxic and hepatorenal toxic potential of dibromochloropropane (DBCP) in drinking water. Fundam **13. 13**(4. 4), 804-15, 804-15.

Johnston RV, Mensik DC, Taylor HW, Jersey GC, Dietz FK (1986). Single-generation drinking water reproduction study of 1,2-dibromo-3-chloropropane in Sprague-Dawley rats. *Bull Environ Contam Toxicol* **37**, 531-7.

Office of Environmental Health Hazard Assessment (OEHHA, 1999). Public Health Goal for 1,2-Dibromo-3-chloropropane (DBCP) in Drinking Water. OEHHA, California Environmental Protection Agency, Sacramento, California, February.

Rao KS, Burek JD, Murray FJ, John JA, Schwetz BA, Bell TJ, Potts WJ, Parker CM (1983). Toxicologic and reproductive effects of inhaled 1,2-dibromo-3-chloropropane in rats. *Fundam Appl Toxicol* **3**, 104-10.

Rao KS, Burek JD, Murray FJ, John JA, Schwetz BA, Beyer JE, Parker CM (1982). Toxicologic and reproductive effects of inhaled 1,2-dibromo-3-chloropropane in male rabbits. *Fundam Appl Toxicol* **2**, 241-51.

U.S. Environmental Protection Agency (U.S. EPA, 1988). Recommendations for and Document of Biological Values for Use in Risk Assessment. U.S. Environmental Protection Agency, Cincinnati, OH, February.

## Bibliography

### Relevant Studies on the Male Reproductive Toxicity of DBCP


Ahmad N, Wisner JR Jr, Warren DW (1988). Morphological and biochemical changes in the adult male rat reproductive system following long-term treatment with 1,2-dibromo-3-chloropropane. *Anat Rec* **222**, 340-9.

Amann RP, Berndtson WE (1986). Assessment of procedures for screening agents for effects on male reproduction: effects of dibromochloropropane (DBCP) on the rat. *Fundam Appl Toxicol* **7**, 244-55.

Berndtson WE, Neefus C, Foote RH, Amann RP (1989). Optimal replication for histometric analyses of testicular function in rats or rabbits. *Fundam Appl Toxicol* **12**, 291-302.

Bjorge C, Wiger R, Holme JA, Brunborg G, Andersen R, Dybing E, Soderlund EJ (1995). In vitro toxicity of 1,2-dibromo-3-chloropropane (DBCP) in different testicular cell types from rats. *Reprod Toxicol* **9**, 461-73.

Bjorge C, Wiger R, Holme JA, Brunborg G, Scholz T, Dybing E, Soderlund EJ (1996). DNA strand breaks in testicular cells from humans and rats following in vitro exposure to 1,2-dibromo-3-chloropropane (DBCP). *Reprod Toxicol* **10**, 51-9.

Brunborg G, Soderlund EJ, Holme JA, Dybing E (1996). Organ-specific and transplacental DNA damage and its repair in rats treated with 1,2-dibromo-3-chloropropane. *Chem Biol Interact* **101**, 33-48.

Chapin, RE, Sloane, RA (1997). Reproductive toxicology. Dibromochloropropane. Environ Health Perspect **105 Suppl 1**, 299-300.

Chayoth R, Kaplanski J, Sror U, Shemi D, Shaked I, Potashnik G, Sod-Moriah UA (1988). The effect of dibromochloropropane (DBCP) on in vitro cyclic AMP levels and testosterone production in rat testes. *Andrologia* **20**, 232-7.

Cohen SZ (1996). Pesticides in ground water in the United States: monitoring, modeling, and risks from the U.S. perspective . *J Environ Sci Health B* **31**, 345-52.

Dybing E, Soderlund EJ, Lag M, Brunborg G, Holme JA, Omichinski JG, Pearson PG, Nelson SD (1991). Testicular metabolism and toxicity of halogenated propanes. *Adv Exp Med Biol* **283**, 471-6.

Eaton M, Schenker M, Whorton MD, Samuels S, Perkins C, Overstreet J (1986). Seven-year follow-up of workers exposed to 1,2-dibromo-3-chloropropane. *J Occup Med* **28**, 1145-50.

Foote RH, Berndtson WE, Rounsaville TR (1986a). Use of quantitative testicular histology to assess the effect of dibromochloropropane (DBCP) on reproduction in rabbits. *Fundam Appl Toxicol* **6**, 638-47.

Foote RH, Schermerhorn EC, Simkin ME (1986b). Measurement of semen quality, fertility, and reproductive hormones to assess dibromochloropropane (DBCP) effects in live rabbits. *Fundam Appl Toxicol* **6**, 628-37.

Generoso WM, Cain KT, Hughes LA (1985). Tests for dominant-lethal effects of 1,2-dibromo-3-chloropropane (DBCP) in male and female mice. *Mutat Res* **156**, 103-8.
Gingell R, Beatty PW, Mitschke HR, Page AC, Sawin VL, Putcha L, Kramer WG (1987). Toxicokinetics of 1,2-dibromo-3-chloropropane (DBCP) in the rat. *Toxicol Appl Pharmacol* **91**, 386-94.

Glass RI, Lyness RN, Mengle DC, Powell KE, Kahn E (1979). Sperm count depression in pesticide applicators exposed to dibromochloropropane. *Am J Epidemiol* **109**, 346-51.
Goldsmith JR (1997). Dibromochloropropane: epidemiological findings and current questions. *Ann N Y Acad Sci* **837**, 300-6.

Goldsmith JR, Potashnik G, Israeli R (1984). Reproductive outcomes in families of DBCP-exposed men. *Arch Environ Health* **39**, 85-9.

Greenwell A, Tomaszewski KE, Melnick RL (1987). A biochemical basis for 1,2-dibromo-3-chloropropane-induced male infertility: inhibition of sperm mitochondrial electron transport activity. *Toxicol Appl Pharmacol* **91**, 274-80.

Heindel JJ, Berkowitz AS, Kyle G, Luthra R, Bruckner JV (1989). Assessment in rats of the gonadotoxic and hepatorenal toxic potential of dibromochloropropane (DBCP) in drinking water. Fundam **13. 13**(4. 4), 804-15, 804-15.

Holme JA, Bjorge C, Trbojevic M, Olsen AK, Brunborg G, Soderlund EJ, Bjoras M, Seeberg E, Scholz T, Dybing E, Wiger R (1998). Effects of chemical-induced DNA damage on male germ cells. *Arch Toxicol Suppl* **20** , 151-60.

Holme JA, Soderlund J, Lag M, Brunborg G, Dybing E (1991). Prevention of 1,2-dibromo-3-chloropropane (DBCP)-induced kidney necrosis and testicular atrophy by 3-aminobenzamide. *Toxicol Appl Pharmacol* **110**, 118-28.

Johnston RV, Mensik DC, Taylor HW, Jersey GC, Dietz FK (1986). Single-generation drinking water reproduction study of 1,2-dibromo-3-chloropropane in Sprague-Dawley rats. *Bull Environ Contam Toxicol* **37**, 531-7.

Kaplanski J, Shemi D, Waksman J, Potashnik G, Sod-Moriah UA (1991). The effects of 1,2-dibromo-3-chloropropane (DBCP) on general toxicity and gonadotoxicity in rats. *Andrologia* **23**, 363-6.

Kapp RW Jr (1979). Detection of aneuploidy in human sperm. *Environ Health Perspect* **31**, 27-31.

Kluwe WM, Lamb JC 4th, Greenwell AE, Harrington FW (1983). 1,2-dibromo-3-chloropropane (DBCP)-induced infertility in male rats mediated by a post-testicular effect. *Toxicol Appl Pharmacol* **71**, 294-8.

Kluwe WM, Weber H, Greenwell A, Harrington F (1985). Initial and residual toxicity following acute exposure of developing male rats to dibromochloropropane. *Toxicol Appl Pharmacol* **79**, 54-68.

Lag M, Soderlund EJ, Brunborg G, Dahl JE, Holme JA, Omichinski JG, Nelson SD, Dybing E (1989). Species differences in testicular necrosis and DNA damage, distribution and metabolism of 1,2-dibromo-3-chloropropane (DBCP). *Toxicology* **58**, 133-44.

Lag M, Soderlund EJ, Omichinski JG, Brunborg G, Holme JA, Dahl JE, Nelson SD, Dybing E (1991). Effect of bromine and chlorine positioning in the induction of renal and testicular toxicity by halogenated propanes. *Chem Res Toxicol* **4**, 528-34 .

Lanham JM (1987). Nine-year follow-up of workers exposed to 1,2-dibromo-3-chloropropane. *J Occup Med* **29**, 488-90.

Leone M, Costa M, Capitanio GL, Palmero S, Prati M, Leone MM (1988). Dibromochloropropane (DBCP) effects on the reproductive function of the adult male rat. *Acta Eur Fertil* **19**, 99-103.

Levine RJ, Blunden PB, DalCorso RD, Starr TB, Ross CE (1983). Superiority of reproductive histories to sperm counts in detecting infertility at a dibromochloropropane manufacturing plant. *J Occup Med* **25**, 591-7.

Levy BS, Levin JL, Teitelbaum DT (1999). DBCP-induced sterility and reduced fertility among men in developing countries: A case study of the export of a known hazard. *Int J Occup Environ Health* **5**, 115.

Lui EM, Wysocki GP (1987). Reproductive tract defects induced in adult male rats by postnatal 1,2-dibromo-3-chloropropane exposure. *Toxicol Appl Pharmacol* **90**, 299-314.

Meistrich ML, Brown CC (1983). Estimation of the increased risk of human infertility from alterations in semen characteristics. *Fertil Steril* **40**, 220-30.

Meistrich ML, Wilson G, Porter KL, Huhtaniemi I, Shetty G, Shuttlesworth GA (2003a). Restoration of spermatogenesis in dibromochloropropane (DBCP)-treated rats by hormone suppression. *Toxicol Sci* **76**, 418-26.

Meistrich ML, Wilson G, Shuttlesworth GA, Porter KL (2003b). Dibromochloropropane inhibits spermatogonial development in rats. *Reprod Toxicol* **17**, 263-71.

Oakberg EF, Cummings CC (1984). Lack of effect of dibromochloropropane on the mouse testis. *Environ Mutagen* **6**, 621-5.

Olsen J (1994). Is human fecundity declining--and does occupational exposures play a role in such a decline if it exists? *Scand J Work Environ Health* **20 Spec No**, 72-7.

Omura M, Hirata M, Zhao M, Tanaka A, Inoue N (1995). Comparative testicular toxicities of two isomers of dichloropropanol, 2,3-dichloro-1-propanol, and 1,3-dichloro-2-propanol, and their metabolites alpha-chlorohydrin and epichlorohydrin, and the potent testicular toxicant 1,2-dibromo-3-chloropropane. *Bull Environ Contam Toxicol* **55**, 1-7.

Osterloh J, Letz G, Pond S, Becker C (1983). An assessment of the potential testicular toxicity of 10 pesticides using the mouse-sperm morphology assay. *Mutat Res* **116**, 407-15.

Pease W, Vandenberg J, Hooper K (1991). Comparing alternative approaches to establishing regulatory levels for reproductive toxicants: DBCP as a case study. *Environ Health Perspect Environ* **91,** 141-55

Potashnik G (1983). A four-year reassessment of workers with dibromochloropropane-induced testicular dysfunction. *Andrologia* **15**, 164-70.

Potashnik G, Abeliovich D (1985). Chromosomal analysis and health status of children conceived to men during or following dibromochloropropane-induced spermatogenic suppression. *Andrologia* **17**, 291-6.

Potashnik G, Goldsmith J, Insler V (1984). Dibromochloropropane-induced reduction of the sex-ratio in man. *Andrologia* **16**, 213-8.

Potashnik G, Phillip M (1988). Lack of birth defects among offspring conceived during or after paternal exposure to dibromochloropropane (DBCP). *Andrologia* **20**, 90-4.

Potashnik G, Porath A (1995). Dibromochloropropane (DBCP): a 17-year reassessment of testicular function and reproductive performance. *J Occup Environ Med* **37**, 1287-92.

Potashnik G, Yanai-Inbar I (1987). Dibromochloropropane (DBCP): an 8-year reevaluation of testicular function and reproductive performance. *Fertil Steril* **47**, 317-23.

Potashnik G, Yanai-Inbar I, Sacks MI, Israeli R (1979). Effect of dibromochloropropane on human testicular function. *Isr J Med Sci* **15**, 438-42.

Rao KS, Burek JD, Murray FJ, John JA, Schwetz BA, Bell TJ, Potts WJ, Parker CM (1983). Toxicologic and reproductive effects of inhaled 1,2-dibromo-3-chloropropane in rats. *Fundam Appl Toxicol* **3**, 104-10.

Rao KS, Burek JD, Murray FJ, John JA, Schwetz BA, Beyer JE, Parker CM (1982).

Toxicologic and reproductive effects of inhaled 1,2-dibromo-3-chloropropane in male rabbits. *Fundam Appl Toxicol* **2**, 241-51.

Saegusa J (1986). Radiomimetic toxicity of 1,2-dibromo-3-chloropropane (DBCP). *Ind Health* **24**, 1-14.

Saegusa J (1987). Age-related susceptibility to dibromochloropropane. *Toxicol Lett* **36**, 45-50.

Saegusa J (1989). Cumulative effects of 1,2-dibromo-3-chloropropane (DBCP) on kidney and testis. *Ind Health* **27**, 49-58.

Saegusa J, Hasegawa H, Kawai K (1982). Toxicity of 1,2-dibromo-3-chloropropane (DBCP). I. Histopathological examination of male rats exposed to DBCP vapour. *Ind Health* **20**, 315-23.

Sandifer SH, Wilkins RT, Loadholt CB, Lane LG, Eldridge JC (1979). Spermatogenesis in agricultural workers exposed to dibromochloropropane (DBCP). *Bull Environ Contam Toxicol* **23**, 703-10.

Sass R (2000). Agricultural "killing fields": the poisoning of Costa Rican banana workers. *Int J Health Serv* **30**, 491-514.

Semenza JC, Tolbert PE, Rubin CH, Guillette LJ Jr, Jackson RJ (1997). Reproductive toxins and alligator abnormalities at Lake Apopka, Florida. *Environ Health Perspect* **105**, 1030-2.

Shaked I, Sod-Moriah UA, Kaplanski J, Potashnik G, Buchman O (1988). Reproductive performance of dibromochloropropane-treated female rats. *Int J Fertil* **33**, 129-33.

Shemi D, Marx Z, Kaplanski J, Potashnik G, Sod-Moriah UA (1988). Testicular damage development in rats injected with dibromochloropropane (DBCP). *Andrologia* **20**, 331-7 .

Shemi D, Sod-Moriah UA, Abraham M, Friedlander M, Potashnik G, Kaplanski J (1989). Ultrastructure of testicular cells in rats treated with dibromochloropropane (DBCP). *Andrologia* **21**, 229-36.

Slutsky M, Levin JL, Levy BS (1999). Azoospermia and oligospermia among a large cohort of DBCP applicators in 12 countries. *Int J Occup Environ Health* **5,** 116-22.

Sod-Moriah UA, Shemi D, Potashnik G, Kaplanski J (1990). Age-dependent differences in the effects of 1,2-dibromo-3-chloropropane (DBCP) on fertility, sperm count, testicular histology and hormonal profile in rats. *Andrologia* **22**, 455-62.

Sod-Moriah UA, Sror U, Shemi D, Potashnik G, Chayoth R, Shaked I, Kaplanski J (1988). Long term effects of dibromochloropropane (DBCP) on male rats' reproductive system. *Andrologia* **20**, 60-6.

Soderlund EJ, Brunborg G, Omichinski JG, Holme JA, Dahl JE, Nelson SD, Dybing E (1988). Testicular necrosis and DNA damage caused by deuterated and methylated analogs of 1,2-dibromo-3-chloropropane in the rat . *Toxicol Appl Pharmacol* **94**, 437-47.

Starr TB, Dalcorso RD, Levine RJ (1986). Fertility of workers. A comparison of logistic regression and indirect standardization. *Am J Epidemiol* **123**, 490-8.

Takahashi W, Wong L, Rogers BJ, Hale RW (1981). Depression of sperm counts among agricultural workers exposed to dibromochloropropane and ethylene dibromide. *Bull Environ Contam Toxicol* **27**, 551-8.

Teitelbaum DT (1999). The toxicology of 1,2-dibromo-3-chloropropane (DBCP): a brief review. *Int J Occup Environ Health* **5, 1**22-6.

Thrupp LA (1991). Sterilization of workers from pesticide exposure: the causes and consequences of DBCP-induced damage in Costa Rica and beyond. *Int J Health Serv* **21**, 731-57.

Warren DW, Ahmad N, Rudeen PK (1988). The effects of fetal exposure to 1,2-dibromo-3-chloropropane on adult male reproductive function. *Biol Reprod* **39**, 707-16.

Warren DW, Wisner JR Jr, Ahmad N (1984). Effects of 1,2-dibromo-3-chloropropane on male reproductive function in the rat. *Biol Reprod* **31**, 454-63.

Whorton D, Foliart D (1988). DBCP: eleven years later. *Reprod Toxicol* **2**, 155-61.

Whorton D, Milby TH, Krauss RM, Stubbs HA (1979). Testicular function in DBCP exposed pesticide workers. *J Occup Med* **21**, 161-6.

Whorton MD, Wong O, Morgan RW, Gordon N (1989). An epidemiologic investigation of birth outcomes in relation to dibromochloropropane contamination in drinking water in Fresno County, California, USA. *Int Arch Occup Environ Health* **61**, 403-7.

Wong O, Whorton MD, Gordon N, Morgan RW (1988). An epidemiologic investigation of the relationship between DBCP contamination in drinking water and birth rates in Fresno County, California. *Am J Public Health* **78**, 43-6.

Yoshida S, Yamada H, Sugawara I, Takeda K (1998). Effect of dibromochloropropane (DBCP) on the hormone receptors of the male rat reproductive system. *Biosci Biotechnol Biochem* **62**, 479-83.