

# 1-BROMOPROPANE

CAS number: 106-94-5

*Synonyms:* n-Propylbromide; Propylbromide

Molecular structure: C<sub>3</sub>H<sub>7</sub>Br

## TLV–TWA, 10 ppm (50 mg/m<sup>3</sup>)

### Summary

A TLV–TWA of 10 ppm (50 mg/m<sup>3</sup>) should provide protection against the potential for neurotoxicity, hepatotoxicity, and reproductive and developmental toxicity in 1-bromopropane-exposed workers. 1-Bromopropane (1-BP) is a potential substitute for solvents used in cleaning, adhesive, and aerosol propellant applications. This document applies to commercial grade bromopropane (99% 1-BP with 0.1%–0.2% 2-bromopropane), not to 2-bromopropane. The recommended TLV–TWA for 1-BP should not be applied to 2-bromopropane. 1-BP exhibited low acute toxicity in rats but produced neurotoxicity, hepatotoxicity, and reproductive and developmental toxicity after repeated exposure. Human studies with 1-BP have not been reported except a case study of a 1-BP-exposed worker who developed polyneuropathy. The no-observed-effect level (NOEL) for hepatotoxicity in the chronic rat study was 200 ppm, and the NOEL for developmental toxicity in rats was less than 100 ppm. All other adverse effects, including neurotoxic and reproductive effects, occurred at higher exposure concentrations. The TLV–TWA for 1-BP should also protect against the potential for all adverse effects, including reproductive or hematopoietic toxicity from the contaminant 2-bromopropane. There is no basis for a skin notation because the dermal LD<sub>50</sub> of 1-BP was >2 g/kg. There are no data upon which to base sensitizer and carcinogenicity notations or support a TLV–STEL for 1-BP.

### Chemical and Physical Properties

Commercial grade 1-BP is a clear, colorless liquid reported to be 99% pure.<sup>(1)</sup> The U.S. Occupational Safety and Health Administration (OSHA) analyzed samples of 1-BP and detected 2-bromopropane (2-BP) at 0.1% to 0.2%.<sup>(2)</sup> Chemical and physical properties include:<sup>(1)</sup>

Molecular weight: 122.99  
Specific gravity: 1.35  
Melting point: –110°C  
Boiling point: 71°C  
Vapor pressure: 146 torr at 20°C  
Flash point: 21°C

Explosion limits: lower: 4.60 vol%, upper: 7.8 vol%

Autoignition temperature: 490°C

Solubility: 2.5 g/L water at 20°C

Conversion factors at 25°C and 760 torr:

1 ppm = 5.03 mg/m<sup>3</sup>, 1 mg/m<sup>3</sup> = 0.2 ppm

### Major Sources of Occupational Exposure

1-BP is a potential substitute for solvents used to clean metals and electronics, in adhesive and coatings applications, and in aerosol propellant applications.<sup>(3)</sup> Airborne 1-BP has an atmospheric lifetime of 15 days,<sup>(4)</sup> much shorter than that of chlorofluorocarbons. Information on the current production of 1-BP in the United States is not available. OSHA<sup>(2)</sup> (1999) estimates that up to 240 million pounds of 1-BP could be produced annually if this substance is used to replace chlorinated solvents in vapor degreasing and cold metal cleaning operations.

### Animal Studies

#### Acute

1-BP exhibits low acute toxicity. The oral LD<sub>50</sub> in Sprague–Dawley rats was greater than 2000 mg/kg.<sup>(5)</sup> The dermal toxicity of 1-BP was investigated in Sprague–Dawley rats at a dose of 2000 mg/kg covered by a semi-occlusive dressing for 24 hours.<sup>(6)</sup> There was no cutaneous reaction to 1-BP and there were no deaths or treatment-related effects, indicating that the dermal LD<sub>50</sub> for 1-BP was greater than 2000 mg/kg.

Wistar rats were exposed to 1-BP vapors for 4 hours in nose-only exposure units.<sup>(7)</sup> The 4-hour LC<sub>50</sub> for 1-BP was 7000 ppm (95% confidence limit [CL], 6800–7200 ppm). Mortality was due to respiratory inflammation and pulmonary edema. The 4-hour LC<sub>50</sub> for 1-BP in SD rats exposed whole body was 14,374 ppm (95% CL, 13,624–15,596 ppm).<sup>(8)</sup> The lowest lethal concentration (LCL<sub>0</sub>) was lower than 11,833 ppm (95% CL, 7,829–13,033 ppm), and the 100% lethal concentration (LC<sub>100</sub>) was greater than 18,186 ppm (95% CL, 16,616–26,632 ppm). These data indicate that the acute toxicity of 1-BP is low. All treated rats exhibited piloerection, decreased

activity, ataxia, and lacrimation within 1 hour after 1-BP exposure, but there were no gross pathological findings in any of the rats.

1-BP did not produce cutaneous reactions in guinea pigs attributable to skin sensitization.<sup>(9)</sup> Animals were treated with 1-BP (25% in paraffin oil) for 10 days and challenged with 1-BP after 12 days without treatment. No clinical signs were observed except skin irritation.

### **Subchronic**

Whole-body inhalation exposure of Sprague–Dawley rats 6 hours/day, 5 days/week over 28 days to 1-BP vapors at 0, 400, 1000, or 1600 ppm produced significant mortality (8/10) at the highest concentration.<sup>(10)</sup> Significant effects were observed in rats exposed to 1000 and 1600 ppm including clinical signs of deteriorating condition, abnormal gait and decreased body weights and food consumption. Other effects included changes in erythrocyte and blood chemistry parameters, increases in liver and kidney weights, and decreases in brain weight. Histopathological lesions were observed in the central nervous system (CNS), urinary system, nasal cavities, sternal bone marrow, lymphoid tissues, and male reproductive system. Exposure at 400 ppm produced histopathological lesions in the CNS. Thus, a no-effect level could not be identified in this study.

Sprague–Dawley rats exposed 6 hours/day, 5 days/week for 8 weeks at 0, 50, 300, or 1800 ppm 1-BP showed decreased body weights and increased liver weights at the highest concentration.<sup>(8)</sup> No other significant changes in food consumption, urinalysis, hematology, or serum biochemistry were observed. All treated rats showed signs of cytoplasmic vacuolization in centrilobular hepatocytes, but these lesions did not exhibit a dose-dependence. Histopathological examinations did not reveal any treatment-related effects in other tissues.

Wistar rats exposed at 1000 and 1500 ppm 1-BP for 4 to 7 weeks exhibited decreases in body weight and motor nerve conduction velocities, increased distal latency of peripheral nerves,<sup>(11)</sup> and neuronal dysfunction in the dentate gyrus of the brain.<sup>(12)</sup> Wistar rats exposed 8 hours/day, 7 days/week for 12 weeks at 200, 400, or 800 ppm 1-BP exhibited dose-dependent decreases in fore limb and hind limb strength, motor nerve conduction velocities, plasma creatine phosphokinase, morphological changes in peripheral nerves and preterminal axons in the gracile nucleus, and increased distal latency of peripheral nerves.<sup>(13)</sup> Ovoid or bubble-like debris of myelin sheaths was prominent in the unraveled muscular branch of the posterior tibial nerve observed in the 800-ppm group but not in the 200- or 400-ppm groups. Dose-dependent decreases in neuron-specific  $\gamma$ -enolase and creatine kinase activities in the cerebrum and brain glutathione and nonprotein sulfhydryl levels

were also observed.<sup>(14)</sup>

Male F344 rats were exposed 8 hours/day, 7 days/week for 3 weeks at 10, 50, 200, or 1000 ppm 1-BP and evaluated for changes in behavior.<sup>(15)</sup> Exposure to 1-BP did not affect memory function or motor coordination but muscle strength decreased dose-dependently. Dose-dependent increases in spontaneous locomotor activity and open-field behavior indicated that 1-BP has excitatory effects on the CNS of male F344 rats.

Sprague–Dawley rats were exposed 6 hours/day, 5 days/week for 13 weeks at 100, 200, 400, or 600 ppm.<sup>(16)</sup> No clinical signs related to treatment were observed. Histopathology revealed centrilobular vacuolization of the liver in the two highest dose groups. No other treatment-related effects were observed. The no-effect level for the liver effects was 200 ppm.

### **Chronic/Carcinogenicity**

No carcinogenicity studies with 1-BP were identified.

### **Genotoxicity**

1-BP was mutagenic with or without metabolic activation toward *Salmonella typhimurium* tester strains TA1535 and TA100 when tested in a closed system, but it was not mutagenic toward strains TA1537, TA1538, or TA98.<sup>(17)</sup> An increase in micronuclei was not observed in Swiss mice given intraperitoneal injections of 600 mg 1-BP/kg (males) or 800 mg 1-BP/kg (females).<sup>(18)</sup> 1-BP did not induce dominant lethal mutations in Sprague–Dawley rats given 400 mg/kg by oral gavage for 5 days.<sup>(19)</sup>

### **Reproductive/Developmental Toxicity**

Repeated chronic inhalation exposure of female Sprague–Dawley rats to 1-BP at concentrations of 250 ppm and higher resulted in reproductive toxicity.<sup>(20)</sup> In this two-generation study, 7-week-old rats were exposed 6 hours/day, 7 days/week for 70 days prior to mating at 0, 100, 250, 500, or 750 ppm 1-BP. Females were not exposed on postnatal day 0 to 4 and only they, not their litters, were exposed during postnatal days 5 to 21. F<sub>1</sub> rats began direct exposure at weaning. Dose-related increases in estrous cycle length at  $\geq 250$  ppm, and follicular cysts and interstitial hyperplasia of ovaries at  $\geq 500$  ppm were observed in F<sub>0</sub> and F<sub>1</sub> females. Reduced fertility and litter size was observed in the F<sub>0</sub> and F<sub>1</sub> generations at  $\geq 250$  ppm. The no-effect level in this study was 100 ppm 1-BP.

Repeated chronic inhalation exposure of male Sprague–Dawley rats<sup>(20)</sup> or Wistar rats<sup>(21)</sup> to 1-BP at concentrations of  $\geq 500$  ppm resulted in reproductive toxicity. Dose-related decreases were observed in normal sperm and sperm motility at  $\geq 500$  ppm and in sperm count at 750 ppm in both F<sub>0</sub> and F<sub>1</sub> males.<sup>(20)</sup> Histopathological changes in

epididymides, prostate, and seminal vesicles and decreased plasma testosterone levels were observed at 800 ppm 1-BP, while reductions in sperm count and motility were observed at  $\geq 400$  ppm.<sup>(21)</sup>

Inhalation exposure of rats to 1-BP produced developmental toxicity.<sup>(22)</sup> Pregnant Sprague–Dawley rats were exposed 6 hours/day from gestational days 6 to 19 at 0, 100, 498, or 996 ppm 1-BP, and fetuses were removed at gestational day 20. Maternal weight gain and food intake decreased at  $\geq 498$  ppm. Decreased fetal weight was observed at all doses. Embryotoxicity was not observed. A dose-related decrease in ossification in the litters was observed at  $\geq 498$  ppm, with a significant increase in bent ribs at 996 ppm. The no-observed-effect level (NOEL) for maternal toxicity was 100 ppm, but decreased fetal weights were observed at this dose.

### Absorption, Distribution, Metabolism, and Excretion

Several studies of the metabolism of 1-BP in rats demonstrated that glutathione conjugation was the major metabolic pathway,<sup>(23,24)</sup> resulting in the urinary excretion of the metabolites n-propylmercapturic acid, 2-hydroxypropylmercapturic acid, and n-propylmercapturic acid sulfoxide. Oxidation of the propyl group also occurred prior to glutathione conjugation.<sup>(24)</sup> Studies with isolated rat hepatocytes showed that 1-BP depleted cellular glutathione.<sup>(25)</sup> Liver enzymes oxidized both 1-BP and 2-BP to their respective alcohols at slow rates.<sup>(26)</sup>

Jones and Walsh<sup>(24)</sup> injected Sprague–Dawley rats intraperitoneally with 200 mg/kg 1-BP and observed a rapid excretion of greater than half of the administered dose in expired air. By hour 100, 25% of the 1-BP dose was excreted in the urine.

Kim et al.<sup>(27)</sup> exposed 7-week-old male and female Sprague–Dawley rats 6 hours/day, 5 days/week for 8 weeks at 50, 300, or 1800 ppm 1-BP. At the highest dose, increases in cytochrome P-450 2E1, glutathione S-transferase, and glutathione peroxidase activity and in protein and lipid peroxides were observed. These results indicate the potential of 1-BP to induce its own metabolism at high exposure concentrations.

### Human Studies

Sclar<sup>(28)</sup> reported a case study of a 19-year-old male who experienced weakness of the lower extremities and the right hand, numbness, and difficulty swallowing and urinating after 2 months of occupational exposure to a degreasing solvent. The solvent contained primarily 1-BP (95.5%) as well as butylene oxide (<0.5%), 1,3-dioxolane (<2.5%), and nitromethane (<0.25%). The levels and routes of exposure were unclear. Although the patient wore gloves (material unspecified), the skin on his right

hand darkened. Nerve conduction tests revealed prolonged distal motor and F response latencies with slower extremity sensory nerve conduction velocities but preserved amplitude response. Magnetic resonance imaging revealed patchy areas of increased T<sub>2</sub> signal in the periventricular white matter and root enhancement in the lumbar region of the spinal cord. Antibodies to infectious agents were not detected in spinal fluid. The author<sup>(28)</sup> concluded that the patient was suffering from a symmetric demyelinating polyneuropathy with CNS involvement. Since similar findings have been reported in 1-BP-exposed rats,<sup>(11–13)</sup> Sclar<sup>(28)</sup> concluded that the human neuropathy may have resulted from 1-BP exposure.

No information on the metabolism or pharmacokinetics of 1-BP in humans was found.

### Toxicity of the Contaminant 2-Bromopropane

2-BP (CASRN 75-26-3) is present as a contaminant in commercial grade bromopropane at 0.1% to 0.2%.<sup>(2)</sup> 2-BP is also known as isopropylbromide; 2-propylbromide; and *sec*-propylbromide. Use of 2-BP as a solvent in the Asian electronics industry was minimized and controlled to an occupational exposure level of 1 ppm<sup>(29)</sup> after South Korean workers experienced hematopoietic and reproductive toxicity.<sup>(30)</sup>

### Animal Studies

#### Acute/Subacute/Chronic

2-BP exhibits low acute toxicity. The oral LD<sub>50</sub> in rats was greater than 2000 mg/kg.<sup>(29)</sup> The 4-hour LC<sub>50</sub> for ICR mice was 31,171 ppm.<sup>(31)</sup>

Male Sprague–Dawley rats were given daily intraperitoneal injections of 125, 250, or 500 mg/kg 2-BP in olive oil for 28 days. The rats exhibited dose-dependent decreases in body weight and testicular weight, with histopathological evidence of testicular necrosis.<sup>(32)</sup> The NOEL was 125 mg/kg body weight. Male Sprague–Dawley rats given oral 2-BP at 100, 330, or 1000 mg/kg daily for 28 days exhibited decreased body and thymus weights at the highest dose. White and red blood cell and platelet numbers were reduced, suggesting an immunotoxic potential of 2-BP.<sup>(33)</sup>

Male Wistar rats were exposed 8 hours/day, 7 days/week for 9 weeks at 300 or 1000 ppm 2-BP. Exposures at 3000 ppm were terminated after 9 to 11 days due to morbidity. The rats exhibited decreased testicular and epididymal weights, decreased sperm count and motility, and decreased erythrocytes and platelets, indicating testicular and hematopoietic toxicity from 2-BP.<sup>(34)</sup> Hypoplasia of bone marrow was observed at exposures of 1000 ppm 2-BP.<sup>(35)</sup> Female Wistar rats exposed at 100, 300, or 1000 ppm 2-BP for 9 weeks developed irregular estrous cycling due to the destruction of primordial follicles and their oocytes.<sup>(36,37)</sup>

Inhalation exposure of Wistar rats 8 hours/day, 7 days/week for 12 weeks at 100 or 1000 ppm 2-BP produced a decrease in motor nerve conduction velocity and prolonged distal latency at the high exposure along with decreases in body and brain weight.<sup>(38)</sup> Similar effects were observed after 5 to 7 weeks exposure at 1000 ppm 1-BP.<sup>(39)</sup>

### **Carcinogenicity**

No carcinogenicity studies with 2-BP were identified.

### **Genotoxicity**

2-BP was mutagenic toward *Salmonella typhimurium* strain TA1535 with or without metabolic activation, but it required metabolic activation to exert mutagenicity toward TA100.<sup>(40)</sup> 2-BP did not induce chromosomal aberrations in Chinese hamster lung cells *in vitro* and did not increase the frequency of micronuclei in the bone marrow of rats treated with intraperitoneal injections of 125, 250, or 500 mg/kg 2-BP daily for 28 days.<sup>(40)</sup>

### **Reproductive/Developmental Toxicity**

Treatment of female Sprague–Dawley rats by intraperitoneal injection of 300, 600, or 900 mg/kg 2-BP for 21 days produced delayed estrous cycle and decreased the number of pups born in the high-dose group.<sup>(41)</sup> Male Sprague–Dawley rats treated with subcutaneous injections of 200, 600, or 1800 mg/kg 2-BP 5 days/week for 5 to 7 weeks exhibited decreased testis weight, decreased sperm concentration and viability, increased sperm abnormalities, decreased serum testosterone concentrations, atrophied seminiferous tubules, and reduced pregnancy and fertility indices when mated with females.<sup>(42)</sup> These data show that 2-BP induces alterations in the neuro-endocrine axis and reproductive tract.

### **Absorption, Distribution, Metabolism, and Excretion**

No information on the metabolism or pharmacokinetics of 2-BP was found.

### **Human Studies**

An outbreak of reproductive and hematopoietic toxicities occurred in Korean electronics workers in 1995 exposed to solvents containing 2-BP that were used as alternatives to chlorofluorocarbons for cleaning tactile switches.<sup>(30,43,44)</sup> Seventeen of 25 female workers showed ovarian dysfunction accompanied by amenorrhea and severe anemia, and 6 of 8 male workers had oligospermia or azospermia.<sup>(30)</sup> The mean ambient 2-BP concentration in the work area was 12.4 ppm, and the 2-BP concentration inside the hood of the cleaning baths was 4141 ppm.<sup>(43)</sup> Some workers had skin contact with 2-BP.

Two of the affected female workers regained normal ovarian function within 2 years following exposure.<sup>(45)</sup> A study of 25 workers in a Chinese 2-BP manufacturing plant found amenorrhea or polymenorrhea in 4 female workers exposed at >10 ppm (TWA) 2-BP.<sup>(46)</sup>

### **TLV Recommendation**

The TLV–TWA recommendation applies to 1-BP containing 2-BP as a contaminant, not to 2-BP. Thus, the recommended TLV–TWA for 1-BP should never be applied to 2-BP.

1-BP exhibited low acute toxicity in rats and produced neurotoxicity,<sup>(13)</sup> hepatotoxicity,<sup>(16)</sup> and reproductive<sup>(20)</sup> and developmental<sup>(22)</sup> toxicity after repeated exposure. Human studies with 1-BP have not been reported except a case study of a 1-BP-exposed worker who developed polyneuropathy.<sup>(28)</sup> The NOEL was 200 ppm for hepatotoxicity in the chronic rat study<sup>(16)</sup> and < 100 ppm for developmental toxicity in rats.<sup>(22)</sup> Decreased fetal weights were observed after exposure of pregnant rats at 100 ppm 1-BP.<sup>(22)</sup> All other adverse effects, including neurotoxic and reproductive effects, occurred at higher exposure concentrations. Therefore, a TLV–TWA of 10 ppm (50 mg/m<sup>3</sup>) should provide protection against the potential for neurotoxicity, hepatotoxicity, and reproductive and developmental toxicity in 1-BP-exposed workers. The TLV for 1-BP should also provide protection against the potential reproductive and hematopoietic toxicities of the impurity 2-BP (0.1%–0.2%).

There is no basis for a skin notation (dermal LD<sub>50</sub> of 1-BP was > 2000 mg/kg<sup>(6)</sup>) or a sensitizer notation.<sup>(9)</sup> No data exist upon which to base a carcinogenicity notation or to support a TLV–STEL for 1-BP.

### **TLV Basis**

CNS; reproductive toxicity (male, female); developmental toxicity

### **References**

1. Fisher Scientific UK: Material Safety Data Sheet for 1-Bromopropane. Fischer Scientific UK, Loughborough, Leicestershire, UK; 2000. Document ID Title OAR-2002-0064: Documents available in public dockets A-2001-07, OAR-2002-0064, and A-91-42 (2000).
2. U.S. Occupational Safety and Health Administration: Nomination of 1-bromopropane (1-BP) and 2-bromopropane (2-BP) for testing by the National Toxicology Program. Directorate of Health Standards Programs, US OSHA, Washington, DC (1999).
3. U.S. Environmental Protection Agency: Protection of stratospheric ozone: notice 14 for significant new alternatives policy program. Fed Reg 65(243):78977–78989 (2000).
4. Nelson Jr DD; Wormhoudt JC; Zahniser MS; et al.: OH Reaction kinetics and atmospheric impact of 1-bromopropane. J Phys Chem 101:4987–4990 (1997).

5. Elf Atochem: Acute oral toxicity in rats: n-Propyl bromide, Study Number 10611 TAR; 1993. Document ID Title OAR-2002-0064: Documents available in public dockets A-2001-07, OAR-2002-0064, and A-91-42. U.S. Environmental Protection Agency, Washington, DC (1993)
6. Elf Atochem: Acute dermal toxicity in rats: n-Propyl bromide, Study Number 13113 TAR; 1995b. Document ID Title OAR-2002-0064: Documents available in public dockets A-2001-07, OAR-2002-0064, and A-91-42. U.S. Environmental Protection Agency, Washington, DC (1995).
7. Elf Atochem: Study of acute toxicity of n-propyl bromide administered to rats by vapour inhalation. Determination of the 50% lethal concentration (LC<sub>50</sub>/4 hours), Study Number 95122; 1997. Document ID Title OAR-2002-0064: Documents available in public dockets A-2001-07, OAR-2002-0064, and A-91-42. U.S. Environmental Protection Agency, Washington, DC (1997).
8. Kim H-Y; Chung Y-H; Jeong J-H.; et al.: Acute and repeated inhalation toxicity of 1-bromopropane in SD rats. *J Occup Health* 41:121–128 (1999).
9. Elf Atochem (1995b) Skin sensitization test in guinea-pigs: n-Propyl bromide, Study Number 12094 TSG; 1995c. Document ID Title OAR-2002-0064: Documents available in public dockets A-2001-07, OAR-2002-0064, and A-91-42. U.S. Environmental Protection Agency, Washington, DC (1995).
10. ClinTrials: A 28-day inhalation toxicity study of a vapor formulation of ALBTA1 in the albino rat, Project Number 91189; 1997a. Document ID Title OAR-2002-0064: Documents available in public dockets A-2001-07, OAR-2002-0064, and A-91-42. U.S. Environmental Protection Agency, Washington, DC (1997).
11. Yu X; Ichihara G; Kitoh J; et al.: Preliminary report on the neurotoxicity of 1-bromopropane, an alternative solvent for chlorofluorocarbons. *J Occup Health* 40, 234-235 (1998).
12. Fueta Y; Ishidao T; Kasai T; et al.: Decreased paired-pulse inhibition in the dentate gyrus of the brain in rats exposed to 1-bromopropane vapor. *J Occup Health* 42:149–151 (2000).
13. Ichihara G; Kitoh J; Yu X; et al.: 1-Bromopropane, an alternative to ozone layer depleting solvents, is dose-dependently neurotoxic to rats in long-term inhalation exposure *Toxicol Sci* 55:116–123 (2000).
14. Wang H; Ichihara G; Ito H; et al.: Dose-dependent biochemical changes in rat central nervous system after 12-week exposure to 1-bromopropane. *Neurotoxicology* 24:199-206 (2003).
15. Honma T; Suda M; Miyagawa M: Inhalation of 1-bromopropane causes excitation in the central nervous system of male F344 rats. *Neurotoxicology* 24:563-575 (2003).
16. ClinTrials: A 13-week inhalation toxicity study of a vapor formulation of ALBTA1 in the albino rat. Project Number 91190; 1997b. Document ID Title OAR-2002-0064: Documents available in public dockets A-2001-07, OAR-2002-0064, and A-91-42. U.S. Environmental Protection Agency, Washington, DC (1997).
17. Barber ED; Donish WH; Mueller KR: A procedure for the quantitative measurement of the mutagenicity of volatile liquids in the Ames *Salmonella*/microsome assay. *Mutat. Res.* 90:31–48 (1981).
18. Elf Atochem: Micronucleus test by intraperitoneal route in mice: n-Propyl bromide, Study Number 12122 MAS; 1995a. Document ID Title OAR-2002-0064: Documents available in public dockets A-2001-07, OAR-2002-0064, and A-91-42. U.S. Environmental Protection Agency, Washington, DC (1995).
19. Saito-Suzuki R; Teramoto S; Shirasu Y: Dominant lethal studies in rats with 1,2-dibromo-3-chloropropane and its structurally related compounds. *Mutat Res* 101:321–327 (1982).
20. WIL Research Laboratories (2001) An inhalation two-generation reproductive toxicity study of 1-bromopropane in rats; 2001. Document ID Title OAR-2002-0064: Documents available in public dockets A-2001-07, OAR-2002-0064, and A-91-42. U.S. Environmental Protection Agency, Washington, DC (2001).
21. Ichihara G; Yu X; Kitoh J; et al.: Reproductive toxicity of 1-bromopropane, a newly introduced alternative to ozone layer depleting solvents, in male rats. *Toxicol Sci* 54:416–423 (2000).
22. Huntingdon Life Sciences (2001) A developmental toxicity study in rat via whole body inhalation exposure, Study Number 98-4141; 2001. Document ID Title OAR-2002-0064: Documents available in public dockets A-2001-07, OAR-2002-0064, and A-91-42. U.S. Environmental Protection Agency, Washington, DC (2001).
23. Barnsley EA; Grenby TH; Young L: Biochemical studies of toxic agents, the metabolism of 1- and 2-bromopropane in rats. *Biochem J* 100:282–288 (1966).
24. Jones AR; Walsh DA: The oxidative metabolism of 1-bromopropane in the rat. *Xenobiotica* 9:763–772 (1979).
25. Khan S; O'Brien PJ: 1-Bromoalkenes as new potent nontoxic glutathione depletors in isolated rat hepatocytes. *Biochem Biophys Res Commun* 179:436–441 (1991).
26. Kaneko T; Kim HY; Wang P-Y; et al.: Partition coefficients and hepatic metabolism *in vitro* of 1- and 2-bromopropanes. *J Occup Health* 39:341–342 (1997).
27. Kim K-W; Kim HY; Park SS; et al.: Gender differences in activity and induction of hepatic microsomal cytochrome P-450 by 1-bromopropane in Sprague–Dawley rats. *J Biochem Mol Biol* 32:232–238 (1999).
28. Sclar G: Case report: encephalomyeloradiculoneuropathy following exposure to an industrial solvent. *Clin Neurol Neurosurg* 101:199N202 (1999).
29. Yu IJ; Kim HY; Lim CH; et al.: The occupational exposure level (OEL) for 2-bromopropane: the first OEL established by Korea. *Appl Occup Environ Hyg.* 14:356–358 (1999c).
30. Park JS; Kim Y; Park DW; et al: An outbreak of hematopoietic and reproductive disorders due to solvents containing 2-bromopropane in an electronic factory, South Korea: epidemiological survey. *J Occup Health* 39:138–143 (1997).
31. Kim HY; Chung YH; Yi KH; et al.: LC<sub>50</sub> of 2-bromopropane. *Ind Health* 34:403–407 (1996).
32. Yu IJ; Chung YH; Lim CH; et al.: Reproductive toxicity of 2-bromopropane in Sprague–Dawley rats. *Scand J Work Environ Health* 23:281–288 (1997).
33. Jeong TC; Lee E-S; Chae W; et al.: Immunotoxic effects of 2-bromopropane in male Sprague-Dawley rats: A 28-day exposure study. *J Toxicol Environ Health A* 65, 383-394 (2002).
34. Ichihara G; Asaeda N; Kumazawa T; et al.: Testicular and hematopoietic toxicity of 2-bromopropane, a substitute for ozone layer-depleting chlorofluorocarbons. *J Occup Health* 39:57–63 (1997).

35. Nakajima T; Shimodaira S; Ichihara G; et al.: 2-Bromopropane-induced hypoplasia of bone marrow in male rats. *J Occup Health* 39:228–233 (1997).
36. Kamijima M; Ichihara G; Kitoh J; et al.: Ovarian toxicity of 2-bromopropane in the non-pregnant female rat. *J Occup Health* 39:144–149 (1997).
37. Yu X; Kamijima M; Ichihara G; et al.: 2-Bromopropane causes ovarian dysfunction by damaging primordial follicles and their oocytes in female rats. *Toxicol Appl Pharmacol* 159:185–193 (1999).
38. Yu X; Ichihara G; Kitoh J; et al.: Effect of inhalation exposure to 2-bromopropane on the nervous system in rats. *Toxicology* 135:87–93 (1999).
39. Yu X; Ichihara G; Kitoh J; et al.: Neurotoxicity of 2-bromopropane and 1-bromopropane, alternative solvents for chlorofluorocarbons. *Environ Res* 85(1):48–52 (2001).
40. Maeng SH; Yu IJ: Mutagenicity of 2-bromopropane. *Ind Health* 35:87–95 (1997).
41. Lim CH; Maeng SH; Lee JY; et al.: Effects of 2-bromopropane on the female reproductive function in Sprague–Dawley rats. *Ind Health* 35:278n284 (1997).
42. Wu X; Faqi AS; Yang J; et al.: Male reproductive toxicity and  $\beta$ -luteinizing hormone gene expression in sexually mature and immature rats exposed to 2-bromopropane. *Human Exp Toxicol* 18:683–690 (1999).
43. Kim Y; Jung K; Hwang T; et al.: Hematopoietic and reproductive hazards of Korean electronic workers exposed to solvents containing 2-bromopropane. *Scand J Work Environ Health* 22:387–391 (1996).
44. Takeuchi Y; Ichihara G; Kamijima M: A review on toxicity of 2-bromopropane: mainly on its reproductive toxicity. *J Occup Health* 39:179–191 (1997).
45. Koh J-M; Kim C-H; Hong SK; et al.: Primary ovarian failure caused by a solvent containing 2-bromopropane. *Eur J Endocrinol* 138:554–556 (1998).
46. Ichihara G; Ding X; Yu X; et al.: Occupational health survey on workers exposed to 2-bromopropane at low concentrations. *Am J Ind. Med* 35:523–531 (1999).