DIBUTYLAMINE

Document History
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I. IDENTIFICATION[1-3]

Chemical Name: Dibutylamine
Synonyms: DNBA; DBA; Di-n-butylamine; N-Butyl-1-butanamine; n-Dibutylamine
CAS Number: 111–92–2
Molecular Formula: C_8-H_{19}-N
Chemical Structure: $(CH_3CH_2CH_2CH_2)_2NH$
UN #: 2248

II. CHEMICAL AND PHYSICAL PROPERTIES[1-4]

Physical State: Liquid (colorless)
Molecular Weight: 129.24
Conversion Factors: 1 ppm = 5.29 mg/m^3;
1 mg/m^3 = 0.189 ppm at 25°C (calculated)
Melting Point: -60 to -59°C (-66 to -76°F)
Boiling Point: 160°C (320°F)
Vapor Pressure: 2.59 mm Hg at 25°C; 1.9–2.2 mm Hg at 20°C
Saturated Vapor Concentration: approx. 2500–2900 (0.3%) ppm at 20°C
Odor Description and Threshold: 0.08 ppm (0.42 mg/m^3) absolute; 0.48 ppm (2.54 mg/m^3) 100% recognition, ammonia-like odor
Flammability Limits: LEL: 1.1 %, UEL: not available
Flash Point: 51.6°C (125°F), open cup; 41–47°C (106–117°F), closed cup
Autoignition Temperature: not available
Specific Gravity: 0.76 at 20°C (water = 1)
Solubility: very soluble in ether and ethanol, soluble in acetone and benzene; moderately soluble in water (3500 mg/l at 25°C)
Reactivity: incompatible with oxidizing materials, strong acids, acid chlorides and acid anhydrides.
Log K_{ow}: 2.83

III. USES AND VOLUMES

Used as a corrosion inhibitor, intermediate for emulsifiers, rubber accelerators, dyes, insecticides, flotation agent, inhibitor for butadiene.[1,2]

IV. TOXICOLOGY DATA

A. Acute Toxicity and Irritancy

1. Oral

LD_{50} = 550 mg/kg (rat, sex and strain not specified)[4]
LD_{50} = 220 mg/kg (rat, female, strain not specified)[1-2]
LD_{50} = 310 mg/kg (rat, male, strain not specified)[2]
LD_{50} = 189 mg/kg (rat, sex and strain not specified)[2-3]
LD_{50} = 290 mg/kg (mouse, sex and strain not specified)[1-3]
LD_{50} = 230 mg/kg (guinea pig, sex and strain not specified)[1-3]

2. Eye Irritation

Exposure to 0.005 ml (250 ug @ 0.05%) dibutylamine to the eyes of rabbits produced severe irritation and corneal injury.[5,2]

3. Skin Absorption

LD_{50} = 770 mg/kg (rabbit, sex and strain not specified)[2-3]
LD_{50} = 1100 mg/kg (rabbit, sex and strain not specified)[1]

4. Skin Irritation

Application of 0.01 ml undiluted dibutylamine to rabbit skin produced severe skin irritation after 24 hrs.[5,2]

5. Skin Sensitization

Dermal sensitization was assessed in a Mouse Ear Swelling Test (MEST), in which 10 CF1 mice received 3 daily topical induction doses of 0.1ml of a 0.1% v/v (in ethanol) solution of dibutylamine. Another (positive control) group of 10 mice was induced with 0.1 ml of 0.5% (w/v) DNCB. Mice were challenged

and rechallenged 7 and 14 days later with 0.1 ml dermal application of a 25% (v/v) solution of dibutylamine to the dorsal and ventral surface of the ear. The right ears of induced mice were used for challenge with the solvent (ethanol) while the left ear was used for challenge with dibutylamine. Swelling in the dibutylamine-challenged ears was compared to ears challenged with the solvent to assess the degree of sensitization. A positive response was considered to be >20% increase in ear thickness/swelling versus the control. One mouse challenged with dibutylamine exhibited a positive sensitization reaction when examined 48 hours post-challenge. However, no sensitization reactions were observed 24 hours after the 7-day challenge, or at either observation time following rechallenge on day 14. DNCB-induced mice exhibited a 60% and 50% sensitization response rate 24 and 48 hours following the 7-day challenge. Dibutylamine was judged negative for dermal sensitization in the MEST.[6,1]

6. Inhalation Toxicity

4-hr LC_{50} = 218 ppm (1.15 mg/l, Sprague-Dawley rat, both sexes, GLP study)[7]

1-hr LC_0 = 573 ppm (3.028 mg/l, Sprague-Dawley rat, both sexes, 0/10 deaths, GLP study)[8]

4-hr LC_0 = 250 ppm (1.323 mg/l, nominal, Wistar rat, sex unspecified, 0/6 deaths)[5]

4-hr LC_{100} = 500 ppm (2.646 mg/l, nominal, Wistar rat, sex unspecified, 6/6 deaths)[5]

RD_{50} = 173 ppm (0.915 mg/l, OF_1 mouse, male, 50% decrease in respiratory rate as index of potency of upper respiratory tract irritation)[9-10]

$RD_{50}TC$ = 106 ppm (0.561 mg/l, OF_1 mouse, male, tracheally cannulated, 50% decrease in respiratory rate as index of potency of lower respiratory tract effects)[9-10]

$RD_{50}TC/RD_{50}$ = 0.6 (ratio < 1.0 indicative of lower airway effects)[9-10]

7. Other

LD_{50} i.p. = 200 mg/kg (mouse, sex and strain not specified)[3]

LD_{50} i.p. = 110 mg/kg (rat, sex and strain not specified)[3]

LD_{50} s.c. = 494 mg/kg (rat, sex and strain not specified)[3]

B. Subacute Toxicity

No data found.

C. Subchronic Toxicity

No data found.

D. Chronic Toxicity/Carcinogenicity

No data found.

In the presence of a nitrosating agent (nitrites), secondary aliphatic amines such as dibutylamine can be converted into the corresponding nitrosamine (N-Nitroso-n-butylamine), which is carcinogenic in animals.[2,15]

E. Developmental/Reproductive Toxicity

No data found.

F. Genotoxicity/Mutagenicity

Dibutylamine was negative when tested in the His^+ reversion assay with *B. subtilis* TKJ5211, and in the Ames assay with *S. typhimurium* strains TA100 and TA98.[11] In another Ames assay with *S. typhimurium* TA100 dibutylamine was also negative with and without exogenous metabolic activation.[12] In a study with cultured Chinese Hamster D-6 cells, exposure to dibutylamine resulted in a significant increase in the frequency of chromosomal aberrations and a slight (< 2-fold) increase in sister chromatid exchange frequency.[13]

Dibutylamine was also tested *in vivo* in a mouse micronucleus assay.[14] Harlan Sprague-Dawley ICR mice (20/sex/group) were administered single oral (gavage) doses of 55, 110, or 220 mg/kg dibutylamine. A concurrent control group was dosed with corn oil. All dibutylamine-treated animals became lethargic following dosing, with some mortality observed at the highest dose (3/20 males, 1/20 females). Bone marrow cells were collected 24, 48, and 72 hours after treatment and examined microscopically for micronucleated polychromatic erythrocytes (PCEs). Reductions in the ratio of PCEs to total erythrocytes of up to 19% relative to the control group were observed in some dibutylamine-treated mice. No significant increase in PCEs was observed in mice of either sex 24, 48 or 72 hours after dosing.

G. Metabolism and Pharmacokinetics

There is no specific information regarding the metabolism of dibutylamine in humans or animals. Amines are readily absorbed from the respiratory and digestive tract. It is unlikely that dibutylamine accumulates in the body.[2,15]

V. HUMAN USE AND EXPERIENCE

Inhalation of monoamine vapors (concentration not reported) has produced headache, nausea, faintness and transient anxiety. Other effects resulting from inhalation of vapor/mist include irritation of the nose, throat, and lungs, sore throat, cough, chest pain and shortness of breath. Exposure to liquid or mist may cause serious skin irritation or burns.[2]

VI. RATIONALE

Dibutylamine is a liquid with an ammonia-like odor. It is a severe eye and skin irritant and prolonged contact can result in permanent injury to eyes and skin. It was negative in a dermal sensitization assay (MEST) in animals. Moderate systemic toxicity has been reported following acute percutaneous exposure in animals. Based on the 4-hr rat LC_{50} value, it should be regarded as acutely toxic when exposures to mists/aerosols occur. Dibutylamine did not produce mutagenic or genotoxic effects in the majority of *in vitro* or *in vivo* assays in which it has been studied. No repeated-dose, reproductive or developmental toxicity studies have been performed with dibutylamine. The RD_{50} of dibutylamine in male mice is 173 ppm. It has been proposed that ($0.03 \times RD_{50}$) should be used to set occupational exposure limits to limit pulmonary irritation.[18] Applying this to the data for dibutylamine yields 5 ppm to prevent respiratory tract irritation, which is consistent with current occupational exposure limits for butylamine.[16-17]

VII. RECOMMENDED OEL

An OEL Guide of 5 ppm (26.5 mg/m^3), ceiling with a "skin" notation is proposed.

VIII. REFERENCES

Databases consulted during this review include: HSDB; CCInfoDisk (Cheminfo); RTECS; TOXLINE; TSCATS; DART

1. **HSDB:** Data Bank Number 310: Dibutylamine. Last revised: 2001/05/16
2. **Cheminfo:** Record 457, n-Dibutylamine. Canadian Centre for Occupational Health and Safety, last revised: 1998.
3. **RTECS:** Record HR7780000, Dibutylamine, last revised: 2000/09.
4. **Ruth, J.H.:** Odor Thresholds and Irritation Levels of Several Chemical Substances: A Review. *Am. Ind. Hyg. Assoc. J. 47*: A142–A151 (1986).
5. **Smyth H.F., C.P. Carpenter, C.S. Weil and U.C. Pozzani:** Range-Finding Toxicity Data. *Arch. Ind. Hyg. Occup. Med. 10*:61–68 (1954).
6. **Virginia Chemicals:** Mouse Ear Swelling Test (Sensitization Assay) of Di-n-butylamine, 05/27/87, EPA Doc. No. 86-87-0000820, OTS0515258 (1987) (summarized in reference 1)
7. **Hardy, C.J. and G.C. Jackson:** Dibutylamine Acute Inhalation Toxicity in Rats, 4-Hour Exposure. Huntingdon Research Centre, 20 Feb. 1987. Report to Pennwalt Corp. EPA Doc. No. 86-870000540, OTS0513618 (1987).
8. **Hardy, C.J. and G.C. Jackson:** Dibutylamine Acute Inhalation Toxicity in Rats, 1-Hour Exposure. Huntingdon Research Centre, 1 May 1987. Report to Pennwalt Corp. EPA Doc. No. 86-870000539, OTS0513617 (1987).
9. **Gagnaire, F., S. Azim, P. Simon, B. Cossec, P. Bonnet and J. de Ceaurriz:** Sensory and Pulmonary Irritation of Aliphatic Amines in Mice: a Structure-Activity Relationship Study. *J. Applied Toxicol. 13(2)*:129–135 (1993).
10. **Gagnaire, F., S. Azim, P. Bonnet, P. Simon, J.P. Guenier and J. de Ceaurriz:** Nansal Irritation and Pulmonary Toxicity of Aliphatic Amines in Mice. *J. Applied Toxicol. 9(5)*:301–304 (1989)
11. **Tanooka, H.:** Development and Applications of *Bacillus subtilis* Test Systems for Mutagens, Involving DNA-Repair Deficiency and Suppressible Auxotrophic Mutations. *Mutat. Res. 42*:19–32 (1977).
12. **Eyre, J.:** Ames Test Results for N-butyl-1-butanamine. 09/15/77. Air Products. EPA Doc. No. 86-870001477, OTS0513639.
13. **Abe, S and M. Sasaki:** Studies on Chromosomal Aberrations and Sister Chromatid Exchanges Induced by Chemicals. *Proc. Jpn. Acad. 53*:46–49 (1977).
14. **Putman, D., R. Gudi and R. Young:** Micronucleus Cytogenetic Assay in Mice. Di-n-Butyl Amine. Microbiological Associates Inc, Oct. 5 1995. Report to Elf Atochem North America, Inc. EPA Doc. No. 86960000057, OTS0958197.
15. **Greim, H., D. Bury, H-J Klimisch, M. Oeben-Negele, and K. Ziegler-Skylakakis:** Toxicity of Aliphatic Amines: Structure-Activity Relationships. *Chemosphere 36(2)*:271–295 (1998).
16. **Mackison, F., R. Stricoff, and L. Partridge Jr.:** NIOSH/OSHA Occupational Health Guidelines for Chemical Hazards (DHHS/NIOSH Pub. No. 81-123) US Govt. Printing Office, Washington DC (1981).
17. **ACGIH:** 2001 *Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices.* American Conference of Governmental Industrial Hygienists, Cincinnati, OH ((2001).
18. **Paustenbach, D.:** Approaches and Considerations for Setting Occupational Exposure Limits for Sensory Irritants: Report of Recent Symposia. *AIHA Journal 62*:697–704 (2001).