n-BUTYL ACRYLATE

Data were last reviewed in IARC (1986) and the compound was classified in *IARC Monographs* Supplement 7 (1987).

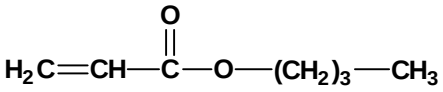
1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 141-32-2
Chem. Abstr. Name: 2-Propenoic acid, butyl ester
IUPAC Systematic Name: Acrylic acid, n-butyl ester
Synonym: Butyl 2-propenoate

1.1.2 *Structural and molecular formulae and relative molecular mass*



$C_7H_{12}O_2$ Relative molecular mass: 128.17

1.1.3 *Chemical and physical properties of the pure substance*

From American Conference of Governmental Industrial Hygienists (1991) unless otherwise noted.

(*a*) *Description*: Colourless, flammable liquid
(*b*) *Boiling-point*: 145°C (Lide, 1997)
(*c*) *Melting-point*: –64.6°C (Lide, 1997)
(*d*) *Solubility*: Very slightly soluble in water (0.14% at 20°C); soluble in ethanol, diethyl ether and acetone
(*e*) *Vapour pressure*: 532 Pa at 20°C; relative vapour density (air = 1), 4.42
(*f*) *Flash-point*: 48.9°C, open cup
(*g*) *Conversion factor*: $mg/m^3 = 5.24 \times ppm$

1.2 Production and use

Production in the United States in 1993 was reported to be 340 035 tonnes (United States International Trade Commission, 1994). Information available in 1995 indicated that it was produced in nine countries (Chemical Information Services, 1995).

n-Butyl acrylate is used in the production of polymers and resins for textile and leather finishes, solvent coatings, adhesives, paints, binders and emulsifiers (Lewis, 1993; United States National Library of Medicine, 1997).

1.3 Occurrence

1.3.1 *Occupational exposure*

According to the 1981–83 National Occupational Exposure Survey (NOES, 1997), approximately 40 000 workers in the United States were potentially exposed to *n*-butyl acrylate (see General Remarks). Occupational exposures may occur in its manufacture and use in the production of polymers and resins, including emulsion polymers for paints.

1.3.2 *Environmental occurrence*

n-Butyl acrylate may be released into the environment in fugitive and stack emissions or in wastewater during its production and use. It has been detected at low levels in ambient and urban air, groundwater and drinking-water samples (United States National Library of Medicine, 1997).

1.4 Regulations and guidelines

The American Conference of Governmental Industrial Hygienists (ACGIH) (1997) has recommended 52 mg/m^3 as the 8-h time-weighted average threshold limit value for occupational exposures to *n*-butyl acrylate in workplace air. Similar values have been used as standards or guidelines in many countries (International Labour Office, 1991). Germany reduced its 8-h time-weighted average MAK value to 11 mg/m^3 (Deutsche Forschungsgemeinschaft, 1998).

No international guideline for *n*-butyl acrylate in drinking-water has been established (WHO, 1993).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

n-Butyl acrylate was tested for carcinogenicity by repeated skin applications in one experiment in male mice; no treatment-related tumour was observed. In a study reported as an abstract, in which male and female rats were exposed to *n*-butyl acrylate by inhalation for two years, no neoplastic effect was observed (IARC, 1986).

3.1 Inhalation exposure

Rat: In a study previously reported in an abstract, four groups of 86 male and 86 female Sprague-Dawley rats, five weeks of age, were administered *n*-butyl acrylate (purity, > 99.5%; main impurities, butyl propionate and isobutyl acrylate) by whole-body inhalation at concentrations of 0, 15, 45 and 135 ppm (0, 86, 258 and 773 mg/m^3) in air for 6 h per day on five days a week for 24 months. Interim kills were performed after 12 months (10 males and 10 females), 18 months (15 males and 15 females) and 24 months (10 males and 10 females). After a further six months, the study was terminated. No dose-related trend in mortality was observed. After 24 months of exposure, the mean cumulative mortality was approximately 20%. During the six-month post-exposure period, the cumulative mortality increased to approximately 45%. Exposure to *n*-butyl acrylate vapour did not lead to an increased frequency of any tumour type in any organ that could be related to the test substance (Reininghaus *et al*., 1991).

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

No data were available to the Working Group.

4.1.2 *Experimental systems*

In-vivo disposition in rats

Sanders *et al.* (1988) administered *n*-butyl [2,3-^{14}C]acrylate to rats orally at doses of 4, 40 and 400 mg/kg bw and intravenously at 40 mg/kg bw. After oral administration, *n*-butyl acrylate was very rapidly absorbed and hydrolysed to acrylic acid, with more than 75% of the dose eliminated as its metabolic end product $^{14}CO_2$. Some 10% of the dose was excreted in the urine, two metabolites being identified as the mercapturic acid *N*-acetyl-*S*-(2-carboxyethyl)cysteine and its sulfoxide. The elimination pattern of ^{14}C was essentially identical at all doses, but additional unidentified ^{14}C peaks were present in the urine at 400 mg/kg. Comparison of the data from the two routes of administration suggested that *n*-butyl acrylate exhibited a first-pass effect after oral dosing, but this was not investigated further. *n*-Butyl acrylate was rapidly and extensively excreted, the tissues being cleared of ^{14}C by 24–72 h. After an initial rapid reduction, a small amount of ^{14}C was retained in whole blood and adipose tissue, possibly by incorporation of ^{14}C via the one-carbon pool.

These findings were confirmed by Linhart *et al.* (1994a) using ^{13}C-labelled *n*-butyl acrylate with nuclear magnetic resonance analysis. These authors also found a significant enrichment of ^{13}C in 3-hydroxypropanoic acid in the urine of rats and, when esterase activity was inhibited with tri-*o*-tolyl phosphate, a third mercapturic acid, *N*-acetyl-*S*-

(butoxycarbonylethyl)cysteine, was found. This is derived from the reverse Michael addition of glutathione across the α,β-unsaturated bond of *n*-butyl acrylate. In further work, Linhart *et al.* (1994b) reported slight increases in the amounts of lactic and acetic acids in rat urine after administration of *n*-butyl acrylate.

In-vitro studies of hydrolysis

Miller *et al.* (1981) showed the rapid hydrolysis of *n*-butyl acrylate in whole homogenate of rat liver, the rate of ester disappearance being the same as that of appearance of acrylic acid. Among a series of acrylate esters, *n*-butyl acrylate was very rapidly hydrolysed by a 5000 × *g* supernatant of the nasal mucosa of mice (Stott & McKenna, 1985). This would lead to high local concentrations of the irritant acrylic acid, consistent with the nasal mucosa being a target organ for toxic effects of this ester when inhaled.

4.2 Toxic effects

4.2.1 *Humans*

The ability of *n*-butyl acrylate to cause allergic contact dermatitis was reported by Kanerva *et al*. (1988, 1996).

4.2.2 *Experimental systems*

No exposure-related clinical signs or lesions of systemic toxicity were observed in male and female Sprague-Dawley rats exposed by inhalation to *n*-butyl acrylate, at concentrations of 0, 15, 45 and 135 ppm [0, 86, 258 and 773 mg/m^3] over 24 months (Reininghaus *et al*., 1991). Atrophy of the neurogenic epithelial cells and hyperplasia of reserve cells were observed in the nasal mucosa of all *n*-butyl acrylate-treated animals. These changes were dose-related and mainly affected the anterior part of the olfactory epithelium. Opacity and neovascularization of the cornea were seen in the group exposed to 135 ppm *n*-butyl acrylate.

4.3 Reproductive and developmental effects

No data were available to the Working Group.

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems* (see Table 1 for references)

In a single study, *n*-butyl acrylate was not mutagenic to *Salmonella typhimurium* in the presence or absence of an exogenous metabolic activation system.

In Chinese hamsters and Sprague-Dawley rats exposed to 4300 mg/m^3 *n*-butyl acrylate by inhalation for 5–6 h per day for four days, no chromosomal damage was observed in single bone-marrow samples taken 5 h after cessation of exposure. [The

Table 1. Genetic and related effects of *n*-butyl acrylate

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	1000	Waegemaekers & Bensink (1984)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	1000	Waegemaekers & Bensink (1984)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	1000	Waegemaekers & Bensink (1984)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	1000	Waegemaekers & Bensink (1984)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	1000	Waegemaekers & Bensink (1984)
MIA, Micronucleus test, Syrian hamster embryo cells *in vitro*	–	NT	10	Wiegand *et al*. (1989)
TCS, Cell transformation, Syrian hamster embryo cells	–	NT	10	Wiegand *et al.* (1989)
CBA, Chromosomal aberrations, Chinese hamster bone-marrow cells *in vivo*	–		820 ppm inh 5–6 h 4 d	Engelhardt & Klimisch (1983)
CBA, Chromosomal aberrations, Sprague-Dawley rat bone-marrow cells *in vivo*	–		820 ppm inh 5–6 h 4 d	Engelhardt & Klimisch (1983)
CBA, Chromosomal aberrations, rat bone-marrow cells *in vivo*	+		300 ip × 1	Fediukovich & Egorova (1991)

[a] +, positive; –, negative; NT, not tested
[b] LED, lowest effective dose; HID, highest ineffective dose; in-vitro tests, µg/mL; in-vivo tests, mg/kg bw/day; inh, inhalation; ip, intraperitoneal

Working Group noted that single samples were tested and the short period between cessation of exposure and sampling.] However, *n*-butyl acrylate induced chromosomal aberrations in the bone marrow of rats dosed by intraperitoneal injection.

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Exposure to *n*-butyl acrylate may occur in its manufacture and its use in the production of polymers and other chemical products. It has been detected at low levels in ambient air and water.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

n-Butyl acrylate was tested in one study in mice by skin application and in one study in rats by inhalation exposure. No carcinogenic effect was observed.

5.4 Other relevant data

n-Butyl acrylate is rapidly absorbed and hydrolysed in experimental animals exposed orally. Exposure of rats to *n*-butyl acrylate vapours leads to hyperplasia of the nasal mucosa. In assays for genotoxicity/mutagenicity considered, results for *n*-butyl acrylate were generally negative.

5.5 Evaluation

No epidemiological data relevant to the carcinogenicity of *n*-butyl acrylate were available.

There is *inadequate evidence* in experimental animals for the carcinogenicity of *n*-butyl acrylate.

Overall evaluation

n-Butyl acrylate is *not classifiable as to its carcinogenicity to humans (Group 3)*.

6. References

American Conference of Governmental Industrial Hygienists (1991) *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 6th Ed., Vol. 1, Cincinnati, OH, pp. 168–169

American Conference of Governmental Industrial Hygienests (1997) *1997 TLVs® and BEIs®*, Cincinnati, OH, p. 17

Chemical Information Services (1995) *Directory of World Chemical Producers 1995/96 Edition*, Dallas, TX

Deutsche Forschungsgemeinschaft (1998) *List of MAK and BAT Values 1996* (Report No. 34), Weinheim, Wiley-VCH Publishers, p. 21

Engelhardt, G. & Klimisch, H. J. (1983) *n*-Butyl acrylate: cytogenetic investigations in the bone marrow of Chinese hamsters and rats after 4-day inhalation. *Fundam. appl. Toxicol.*, **3**, 640–641

Fediukovich, L. V. & Egorova, A. B. (1991) Genotoxic effect of acrylates. *Gig. Sanit.*, 62–64 (in Russian)

IARC (1986) *IARC Monographs on the Evaluation of the Carcinogenic Risks of Chemicals to Humans*, Vol. 39, *Some Chemicals Used in Plastics and Elastomers*, Lyon, pp. 67–79

IARC (1987) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Suppl. 7, *Overall Evaluations of Carcinogenicity: An Updating of* IARC Monographs *Volumes 1 to 42*, Lyon, p. 59

International Labour Office (1991) *Occupational Exposure Limits for Airborne Toxic Substances*, 3rd Ed. (Occupational Safety and Health Series No. 37), Geneva, pp. 62–63

Kanerva, L., Estlander, T. & Jolanki, R. (1988) Sensitization to patch test acrylates. *Contact Derm.*, **18**, 10–15

Kanerva, L., Lauerma, A., Estlander, T., Alanko, K., Henriks-Eckerman, M.-L. & Jolanki, R. (1996) Occupational allergic contact dermatitis caused by photobonded sculptured nails and a review of (meth) acrylates in nail cosmetics. *Am. J. contact Derm.*, **7**, 109–115

Lewis, R.J., Jr (1993) *Hawley's Condensed Chemical Dictionary*, 12th Ed., New York, Van Nostrand Reinhold, p. 181

Lide, D.R., ed. (1997) *CRC Handbook of Chemistry and Physics*, 78th Ed., Boca Raton, FL, CRC Press, p. 3-290

Linhart, I., Hrabal, R., Smejkal, J. & Mitera, J. (1994a) Metabolic pathways of 1-butyl[3-^{13}C]-acrylate. Identification of urinary metabolites in rat using nuclear magnetic resonance and mass spectroscopy. *Chem. Res. Toxicol.*, **7**, 1–8

Linhart, I., Vosmanska, M. & Smejkal, J. (1994b) Biotransformation of acrylates. Excretion of mercapturic acids and changes in urinary carboxylic acid profile in rats dosed with ethyl and 1-butyl acrylate. *Xenobiotica*, **24**, 1043–1052

Miller, R.R., Ayres, J.A., Rampy, L.W. & McKenna, M.J. (1981) Metabolism of acrylate esters in rat tissue homogenates. *Fundam. appl. Toxicol.*, **1**, 410–414

NOES (1997) *National Occupational Exposure Survey 1981-83*, Unpublished data as of November 1997, Cincinnati, OH, United States Department of Health and Human Services, Public Health Service, National Institute for Occupational Safety and Health

Reininghaus, W., Koestner, A. & Klimisch, H.-J. (1991) Chronic toxicity and oncogenicity of inhaled methyl acrylate and *n*-butyl acrylate in Sprague-Dawley rats. *Food chem. Toxicol.*, **29**, 329–339

Sanders, J.M., Burka, L.T. & Matthews, H.B. (1988) Metabolism and disposition of *n*-butyl acrylate in male Fischer rats. *Drug Metab. Disp.*, **16**, 429–434

Stott, W.T. & McKenna, M.J. (1985) Hydrolysis of several glycol ether acetates and acrylate esters by nasal mucosal carboxylesterase *in vitro*. *Fundam. appl. Toxicol.*, **5**, 399–404

United States International Trade Commission (1994) *Synthetic Organic Chemicals: US Production and Sales, 1993* (USITC Publ. 2810), Washington DC, United States Government Printing Office, p. 3-85

United States National Library of Medicine (1997*) Hazardous Substances Data Bank (HSDB)*, Bethesda, MD [Record No. 305]

Waegemaekers, T.H. & Bensink, M.P. (1984) Non-mutagenicity of 27 aliphatic acrylate esters in the Salmonella-microsome test. *Mutat. Res.*, **137**, 95–102

WHO (1993) *Guidelines for Drinking Water Quality*, 2nd Ed., Vol. 1, *Recommendations*, Geneva

Wiegand, H.J., Schiffman, D. & Henschler, D. (1989) Non-genotoxicity of acrylic acid and *n*-butyl acrylate in a mammalian cell system (SHE cells). *Arch. Toxicol.*, **63**, 250–251