# JACC Report

# No 27

# *n*-Butyl Acrylate
# CAS No. 141-32-2

# August 1994

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ECETOC

# Joint Assessment of Commodity Chemicals No. 27

## *n*-Butyl Acrylate

## CAS No. 141-32-2

August 1994

European Centre for Ecotoxicology
and Toxicology of Chemicals

Avenue E. Van Nieuwenhuyse 4, (Bte. 6)
B - 1160 Brussels, Belgium

# JACC REPORT

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# Joint Assessment of Commodity Chemicals, No. 27

## *n*-Butyl Acrylate

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# ECETOC JACC Report No. 27

# THE ECETOC SCHEME FOR THE JOINT ASSESSMENT OF COMMODITY CHEMICALS

This report has been produced as part of the ECETOC programme for preparing critical reviews of the toxicology and ecotoxicology of selected existing industrial chemicals.

In the programme, commodity chemicals, that is those produced in large tonnage by several companies and having widespread and multiple uses, are jointly reviewed by experts from a number of companies with knowledge of the chemical. It should be noted that in a JACC review only the chemical itself is considered; products in which it appears as an impurity are not normally taken into account.

ECETOC is not alone in producing such reviews. There are a number of organisations that have produced and are continuing to write reviews with the aim of ensuring that toxicological knowledge and other information are evaluated. Thus a Producer, Government Official or Consumer can be informed on the up-to-date position with regard to safety, information and standards. Within ECETOC we do not aim to duplicate the activities of others. When it is considered that a review is needed every effort is made to discover whether an adequate review exists already; if this is the case the review is checked, its conclusions summarised and the literature published subsequent to the review assessed. To assist ourselves and others working in this field we publish annually a summary of international activities incorporating work planned, in hand, or completed on the review of safety data for commodity chemicals. Interested readers should refer to our Technical Report No. 30 entitled "Existing Chemicals: Literature Reviews and Evaluations".

This document presents a critical assessment of the toxicology and ecotoxicology of *n*-Butyl acrylate (CAS No. 141-32-2).

# *n*-BUTYL ACRYLATE.

## CONTENTS

# SECTION 1. SUMMARY AND CONCLUSIONS

*n*-Butyl acrylate (BA) is an industrial chemical used in the manufacture of polymers and copolymers. At room temperature it is a clear liquid with a pungent, fruity odour. Production in the USA, Western Europe and Japan was 440 kt in 1987.

The majority (90%) of BA released into the environment is expected to enter into the atmosphere, where its half-life has been estimated to be 12.6 hours. In water, any BA which is not volatilised is expected to biodegrade under aerobic conditions. No data are available on the fate of BA in soils.

The acute toxicity of BA to aquatic organisms is > 1 mg/l, it is readily biodegradable and does not bioaccumulate. Thus BA need not be classified as dangerous to the environment according to the 7th amendment of Council Directive 67/548/EEC. Because of its distribution into the environment and biodegradability in aquatic systems, toxic concentrations of BA are unlikely to occur in water during normal use.

BA is irritant to the skin, eyes and mucous membranes, and may cause skin sensitisation in susceptible animals and human beings. Cross-sensitisation may also occur to other acrylic acid esters. Studies in experimental animals have shown that BA is of low oral and dermal toxicity, and moderately toxic via the inhalation route. Following prolonged or repeated exposure, the most common effects observed are those associated with the irritating properties of BA. No systemic toxic effects have been reported.

BA is rapidly absorbed following oral and inhalation exposure. Disposition of BA, as judged by the distribution of radio-activity, is rapid and widespread throughout the body following oral, i.v., i.p., and inhalation exposure. Two metabolic routes have been identified for BA; hydrolysis of the ester linkage to form acrylic acid and 1-butanol, and conjugation with glutathione (non-protein sulphydryl groups) to form mercapturic acids. Hydrolysis, the major route, is mediated by carboxylesterase. The end products, acrylic acid and butyl alcohol are further metabolised to carbon dioxide and water. The irritation produced at the site of first contact, in particular respiratory tissue, is thought to be related to esteratic hydrolysis liberating acrylic acid. The minor route, glutathione conjugation, can occur either by direct chemical Michael addition or enzymatically via a glutathione transferase. The sulphydryl conjugates produced are then rapidly excreted in the urine.

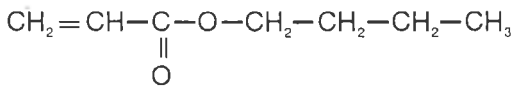
By inhalation, BA is maternally toxic and embryotoxic at concentrations of 135 ppm and above in the rat; the NOEL is 25 ppm. By the oral route, BA was maternally toxic and embryotoxic in mice at

1,000 mg/kgbw/d and above; the NOEL is 100 mg/kgbw/d. At the currently accepted occupational exposure levels, BA represents no reproductive risk to man.

BA has been tested in a battery of genotoxicity tests, both *in vitro* and *in vivo*. No genotoxic potential was found. Chronic inhalation and dermal assays with BA showed no evidence of carcinogenic potential. Therefore, BA does not pose a genotoxic or carcinogenic hazard to man.

# SECTION 2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS

## 2.1 IDENTITY

| | |
|---|---|
| Name: | *n*-Butyl acrylate |
| IUPAC name: | 2-Propenoic acid, *n*-butyl ester |
| Synonyms: | Butyl acrylate |
| | Acrylic acid, *n*-butyl ester |
| D: | *n*-Butylacrylat |
| | 2-Propensäure, Butyl-ester |
| DK: | Butylacrylat |
| F: | Acrylate de *n*-butyle |
| EL: | Ακρυλικός *n*-βουτυλεστέρας |
| I: | Acrilato de *n*-butilo |
| | *n*-Butilacrilato |
| NL: | *n*-Butylacrylaat |
| ES: | Acrilato di *n*-butilo |
| CAS name: | 2-Propenoic acid, *n*-butyl ester |
| CAS registry No: | 141-32-2 |
| EEC No: | 607-062-00-3 |
| EINECS No: | 205-480-7 |
| Formula: | $C_7H_{12}O_2$ |
| Molecular mass: | 128.17 |
| Structural formula: |  |

## 2.2 PHYSICAL AND CHEMICAL PROPERTIES

*n*-Butyl acrylate (BA) is a clear, flammable liquid with a pungent, fruity odour. It is soluble in water and miscible with most organic solvents at any ratio. Data on the physical and chemical properties of BA are given in Table 1.

A typical commercial sample of BA has a purity of ≥ 99.5% (w/w) and may contain the following specified impurities: water (≤ 0.05% w/w) and acid (≤ 0.01% w/w, calculated as acrylic acid) (BASF, 1990).

BA polymerises readily under the influence of heat or light and by catalysis (e.g. metals). This is a strongly exothermic reaction. To prevent uncontrolled polymerisation, the monomer is stabilised by the addition of an inhibitor such as the monomethyl ether of hydroquinone (MeHQ) at levels of 15 ±5 ppm (BASF, 1990) (Section 3.2).

## 2.3 CONVERSION FACTORS

Conversion factors for concentrations of EA in air at 20°C and 1,013 hPa are:

- 1 ppm = 5.33 mg/m$^3$
- 1 mg/m$^3$ = 0.188 ppm

## 2.4 ANALYTICAL METHODS

### 2.4.1 Environmental Media

The analysis of BA in workplace air has been undertaken by GC methods (Samimi and Falbo, 1982; Kollar *et al*, 1987). For trace analysis pre-concentration on activated carbon, then desorption with ether and GC analysis can give a detection limit of 3.4 ppb (Džandžannajan, 1988). A lower limit of detection (0.1 ppb) has been achieved by Yocom *et al* (1984).

Standard charcoal tubes have been used for adsorption of BA, at levels of approximately 50 mg/m$^3$ (9.4 ppm), followed by desorption with $CS_2$ and GC analysis (Samimi and Falbo, 1985). Passive dosimeters can also be used for the measurement of worker exposure (Samimi and Falbo, 1983;

**Table 1 Physical and Chemical Properties**

| Parameter, units | Value | Reference |
|---|---|---|
| Melting temperature, °C, approximately | -64 | BASF, 1990 |
| Boiling temperature, °C at 1,013 hPa, approximately | 148 | BASF, 1990 |
| Heat of polymerisation, kJ/kg | 278.9 | BASF, 1990 |
| Relative density $D_4^{20}$ (density of water at 4°C is 1,000 kg/m$^3$) | 0.898 | BASF, 1990 |
| Viscosity, mPa· s at 20°C | 0.75 | BASF, 1990 |
| Refractive index $n_D$ at 20°C | 1.415<br>1.418 | BASF, 1990<br>Elf Atochem, 1990 |
| Vapour pressure at 20°C | 4.3 | BASF, 1990 |
| Vapour density at 20°C (air=1) | 4.4 | Elf Atochem, 1990 |
| Threshold odour concentration, ppm | 0.1-0.12<br>0.035 | ACGIH, 1980<br>Amoore and Hautala, 1983 |
| Surface tension, mN/m at 20°C | 26.5<br>20 | BASF, 1986<br>Weiss, 1986 |
| Solubility in water, g/kg at 25°C | 2 | BASF, 1990 |
| Solubility of water in BA, g/kg at 25°C | 7 | BASF, 1990 |
| Miscible with most organic solvents | Yes | BASF, 1990 |
| Fat solubility, mg/100 g at 37°C | No data | |
| Partition coefficient, log $P_{ow}$ (octanol/water) at 20°C | 2.36<br>2.38-2.44 | Tanii and Hashimoto, 1982 (measured)<br>BASF, 1988 (measured) |
| Partition coefficient, log $K_{oc}$ (organic carbon/water) at 20°C | No data | |
| Henry's Law constant, Pa· m$^3$/mol at 20°C | 39 | BASF, 1993 (calculated) |
| Flash point, °C, closed cup | 36.5<br>41 | BASF, 1990<br>Elf Atochem, 1990 |
| Explosion limits, % at 35-73.4°C | 1.1-7.8<br>1.6-9.9 | BASF, 1990<br>Elf Atochem, 1990 |
| Auto-flammability, ignition temperature, °C | 267 | BASF, 1990 |

Kollar and Kemka, 1983; Kollar *et al*, 1987; Samimi, 1987). Qualitative determination of BA in air can be undertaken with Draeger tubes (Kühn and Biret, 1986).

No methods are available for the determination of EA in water, soil and sediments.

### 2.4.2 Biological Media

A high-pressure liquid chromatography (HPLC) method for the determination of BA and its metabolites in animal tissues and urine has been described by Sanders *et al* (1988). No detection limit was given for this method.

# SECTION 3. PRODUCTION, STORAGE, TRANSPORT AND USE

## 3.1 PRODUCTION

The most common BA production method is direct esterification of acrylic acid with *n*-butanol.

The quantities produced in the USA, Western Europe and Japan increased from 330 kt/y in 1984 (SRI International, 1987) to approximately 440 kt in 1987 (SRI International, 1990).

## 3.2 STORAGE AND TRANSPORT

To prevent polymer formation during storage and shipping, a stabiliser such as MeHQ is added (Section 2.2). The effectiveness of phenolic inhibitors requires the presence of oxygen, and the monomer must therefore be stored in the dark, under air (not under inert gases) and at a temperature below 25°C if peroxide and polymer formation is to be minimised.

BA is normally stored or shipped in containers made of mild or stainless steel, or aluminium.

## 3.3 USE

BA is used to prepare homopolymers and copolymers with other monomers such as acrylic acid and its salts, amides and esters; methacrylates, acrylonitrile, maleic acid esters, vinyl acetate, vinyl chloride, vinylidene chloride, styrene, butadiene, unsaturated polyesters and drying oils. These polymers and copolymers are used in a variety of products as dispersions or solutions. As BA readily enters into addition reactions with numerous organic and inorganic compounds, it is a valuable starting product for chemical synthesis (BASF, 1990).

The quantities of BA consumed in 1988 were 254 kt in the USA and 50 kt in Japan. The consumption in Western Europe was not reported, but was estimated to be 165 kt in 1987 (SRI International, 1990).

The consumption pattern of acrylates in Western Europe in 1984 for different applications is shown in Table 2.

**Table 2** **Consumption Pattern of Acrylates in 1984 in Western Europe**
(SRI International, 1990)

| Application | % |
|---|---|
| Surface coatings | 35 - 40 |
| Textiles, non-wovens, leather | 10 - 15 |
| Adhesives | 15 |
| Paper coatings | 15 - 20 |
| Fibres and plastics comonomer | 10 |
| Other | 10 |

# SECTION 4. EMISSIONS, ENVIRONMENTAL DISTRIBUTION AND TRANSFORMATION

## 4.1 EMISSIONS

### 4.1.1 Emissions During Production

BA is normally manufactured in a closed plant. BA vapours from vented equipment and tanks are destroyed by flaring, as are vapours resulting from processing. Quantitative information is not available.

Waste-water produced during manufacture and processing of BA is handled in waste-water treatment plants (Section 4.3.4).

### 4.1.2 Emissions During Use

BA is used in large quantities for the manufacture of polyacrylates, as dispersions, solutions and resins. Polyacrylates are used in different applications such as paints, lacquers and adhesives. Emissions of BA from the use of these products has been estimated at 25 t/y in Western Europe, based on a residual monomer content of 500 ppm. There is no estimate of the amount of residual monomer escaping into the hydrosphere from the use of polyacrylates.

BA may enter the geosphere from dumped industrial waste sludge although there are no data to support this assumption (Legiec and Kosson, 1988).

## 4.2 ENVIRONMENTAL DISTRIBUTION

Data on the environmental distribution of BA are not available.

Using the fugacity model of Mackay and Patterson (1981), a theoretical distribution can be calculated indicating that the majority (90.2%) of EA released into the environment will enter the atmosphere. Most of the remainder will be found in the water-phase, with negligible amounts in soil and sediment (Table 3).

**Table 3 Estimated Partitions Between Environmental Compartments at 25°C**

| Compartment | % |
|---|---|
| Air | 90.2 |
| Water | 9.5 |
| Soil | 0.2 |
| Sediment | 0.1 |

## 4.3 ENVIRONMENTAL FATE AND BIOTRANSFORMATION

### 4.3.1 Atmospheric Fate

BA is susceptible to photodegradation in the presence of hydroxyl radicals (· OH) and ozone molecules ($O_3$). An atmospheric half-life of 12.6 hours was estimated at an atmospheric concentration of $5x10^5$ · OH/$cm^3$ and $7x10^{11}$ $O_3$/$cm^3$ (Atkinson, 1987).

### 4.3.2 Aquatic Fate

BA is moderately soluble in water at ambient temperature (Table 1). Based on a Henry's Law constant of 39 Pa·$m^3$/mol, BA is likely to volatilise from the aquatic environment into the atmosphere.

BA hydrolyses slowly at pH ≤ 7, whereas under alkaline conditions hydrolysis is rapid (Table 4).

**Table 4 Hydrolysis Half-life of $^{14}$C-BA at 25°C** (Walsh, 1990)

| pH | $t_{½}$ | Units |
|---|---|---|
| 3 | 2,800 | d |
| 7 | 1,100 | d |
| 11 | 243 | min |

### 4.3.3 Terrestrial Fate

No data are available.

Under normal conditions, BA can be assumed to evaporate into the atmosphere.

### 4.3.4 Biodegradation

The $BOD_5$ of BA has been determined to be 900-920 mg $O_2$/g. The degree of mineralisation, i.e. the ratio BOD/COD, was 50-56% (Flaherty, 1989; BASF, 1991). Thus, BA can be considered as readily biodegradable according to the 7th amendment of Council Directive 67/548/EEC (EEC, 1992).

### 4.3.5 Bioaccumulation

Log $P_{ow}$-values of between 2.36-2.44 (Table 1) indicate a low bioaccumulation potential for BA. Using the equation: $\log BCF = 0.76 \log P_{ow} - 0.23$ (Lyman *et al*, 1990), a theoretical bioaccumulation factor of 37-42 can be estimated.

### 4.3.6 Evaluation

The majority (90%) of BA released into the environment is expected to enter into the atmosphere, where its half-life has been estimated to be 12.6 hours. In water, any BA which is not volatilised is expected to biodegrade under aerobic conditions. No data are available on the fate of BA in soils. BA is not expected to bioaccumulate.

# SECTION 5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

## 5.1 ENVIRONMENTAL LEVELS

### 5.1.1 Air

BA was detected in ambient air samples at 108 locations near industrial sites in New Jersey and Staten Island, NY. The BA concentration in the air near an industrial site of Newark NJ was 8.2 ppb (Pellizzari, 1977).

Measurements of the BA concentration in indoor air of 2 public buildings in the USA yielded very low levels, between < 0.10 ppb (detection limit) and 3.1 ppb (maximum) (Hijazi *et al*, 1983; Yocom *et al*, 1984). The source of these low BA concentrations could not be identified.

### 5.1.2 Water

In the USA, a single finding of 0.234 mg BA/l was reported in the eluate of Soxhlet-extracted core samples taken in 1986 from a lagoon with deposited industrial sewage sludge at a depth of 1.2-1.8 m. BA could not be detected in core samples taken at a depth of 2.4-4.3 m (Legiec and Kosson, 1988). This exceptional finding is not considered to represent normal BA levels in water.

### 5.1.3 Soil

No data are available.

### 5.1.4 Biological Media

No data are available.

## 5.2 OCCUPATIONAL EXPOSURE LEVELS AND HYGIENE STANDARDS

### 5.2.1 Occupational Exposure

Concentrations of BA in work place areas (Table 5) lie mostly below the occupational exposure limits (Table 6).

**Table 5 Personal Exposure Levels at the Workplace**

| Job category | Country | Number of samples | Concentration (ppm) | Reference |
|---|---|---|---|---|
| Production | ČSFR | - | ≤9.4[a] | Kuželová *et al*, 1981 |
| Production | ČSFR | 32 | 1-30[b] | Kollar *et al*, 1988 |
| Production | Germany | - | <0.009-1[c] | BASF, 1992 |
| Production of polymers and copolymers | Germany | - | <0.009[d] | BASF, 1992 |
| Copolymerisation with vinylacetate | USA | 5<br>3 | <0.07<br><0.07-0.92 | Belanger and Coye, 1981 |
| Copolymerisation with vinylacetate | USA | 5 | <0.1- <0.2 | Boxer and Reed, 1983 |
| Copolymerisation with styrene | USA | 200<br>285 | <0.001-0.270<br><0.001-0.525 | Samimi and Falbo, 1982 |
| Discharging gantry | USA | 11<br>18 | <0.001-0.350<br><0.001-0.166 | Samimi and Falbo, 1982 |

a Calculated from ≤50 mg/m$^3$
b Calculated from 6-161 mg/m$^3$
c Calculated from <0.05-6 mg/m$^3$
d Calculated from <0.05 mg/m$^3$

### 5.2.2 Hygiene Standards

Most industrialised countries have adopted occupational exposure limit values (Table 6).

**Table 6 Occupational Exposure Limit Values**

| Country | TWA[a] | | STEL[b] | | Reference |
|---|---|---|---|---|---|
| | (ppm) | (mg/m$^3$)[c] | (ppm) | (mg/m$^3$)[d] | |
| Australia | 10 | 55 | - | - | ILO, 1991 |
| Austria | 10 | 55 | - | - | DFG, 1992 |
| Belgium | 10 | 52 | - | - | ACGIH, 1992 |
| ČSFR | - | 5 | - | 10 | ILO, 1991 |
| Denmark | 10 | 55 | - | - | ILO, 1991 |
| Finland | 10 | 55 | 20 | 110 | ILO, 1991 |
| France | 10 | 55 | - | - | INRS, 1988 |
| Germany | 10 | 55 | - | - | DFG, 1992 |
| Hungary | - | 20 | - | 40[d] | ILO, 1991 |
| Italy | 10 | 52 | - | - | ACGIH, 1992 |
| Netherlands | 10 | 55 | - | - | Arbeidsinspectie, 1991 |
| Norway | 10 | 55 | - | - | Arbeidstylsynet, 1990 |
| Sweden | 10 | 50 | 15 | 80 | AFS, 1990 |
| Switzerland | 10 | 55 | 20 | 110 | ILO, 1991 |
| UK | 10 | 55 | - | - | UK-HSE, 1992 |
| USA | 10 | 52 | - | - | ACGIH, 1992 |
| | - | 55 | - | - | NIOSH/OSHA, 1986 as quoted in ILO, 1991 |
| USSR | - | - | - | 10 | ILO, 1991 |

a Time-weighted average concentration (8-h working period)
b Short-term exposure limit (15 min, unless specified otherwise)
c Official values; some countries use different conversion factors and/or other ambient temperature
d Ceiling value

# SECTION 6. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

## 6.1 MICRO-ORGANISMS

The threshold level for inhibition of bacterial growth ($EC_3$) for *Pseudomonas putida* was 80 mg BA/l after exposure for 16 hours (Bringmann and Kühn, 1977).

Blum and Speece (1991) reported 24-h $IC_{50}$ values of 37.8, 151 and 480 mg BA/l for *Nitrosomas*, methanogens and aerobic heterotrophs respectively.

## 6.2 AQUATIC ORGANISMS

The available data regarding the acute and chronic toxicity of BA are shown in Tables 7, 8 and 9.

Within single cell organisms (Table 7), the saprozoic flagellate *Chilomonas paramecium* proves to be the most sensitive organism, displaying a threshold level of 3.5 mg BA/l. Both the holozoic flagellate and ciliate are less sensitive.

**Table 7 Aquatic Toxicity - Single-Cell Organisms**

| Test species | Effect/ parameter | Time (h) | Concentration (mg BA/l) | Reference |
|---|---|---|---|---|
| | **Growth inhibition** | | | |
| *Chilomonas paramecium* | $EC_5$ | 48 | 3.5 | Bringmann and Kühn, 1980 |
| *Entosiphon sulcatum* | $EC_5$ | 72 | 50 | Bringmann, 1978 |
| *Uronema parduczi* | $EC_5$ | 20 | 21 | Bringmann and Kühn, 1981 |

Acute tests with higher organisms yielded $LC_{50}$ ($EC_{50}$) concentrations ranging from 5 mg BA/l for the goldfish (*Carassius auratus*) to 45 mg BA/l for *Daphnia magna*. $LC_0$ ($EC_0$) values were 7.8 mg BA/l for *D. magna* and 9 mg BA/l for the golden orfe (*Leuciscus idus melanotus*) (Table 8).

Long-term data are available for algae only (Table 9). *Scenedesmus quadricauda* shows growth retardation at concentrations of 9 mg BA/l and above when tested during an 8-d period. The blue-

green alga *Microcystis* is more sensitive, exhibiting an $EC_3$ for growth inhibition of 1.3 mg BA/l after 8 days.

**Table 8 Aquatic Toxicity - Higher Organisms**

| Test species | Effect/ parameter | Time (d) | Concentration (mg/l) | Reference |
|---|---|---|---|---|
| | **Immobility** | | | |
| *Daphnia magna* | $EC_0$ | 1 | 7.8 | Bringmann and Kühn, 1982 |
| | $EC_{50}$ | 1 | 45 | |
| | $EC_{100}$ | 1 | 125 | |
| *Daphnia magna* | $EC_{50}$ | 2 | 8.2 | Burgess, 1990 |
| | **Lethality** | | | |
| *Leuciscus idus melanotus* | $LC_0$ | 2 | 9 | Juhnke and Lüdemann, 1978 |
| | $LC_{50}$ | | 23 | |
| | $LC_{100}$ | | 45 | |
| *Carrassius auratus* | $LC_{50}$ | 3 | 5 | Reinert, 1987 |
| *Onkorynchus mykiss (Salmo gairdneri)* | $LC_{50}$ | 4 | 5.2 | Bowman, 1990 |

**Table 9 Aquatic Toxicity - Algae and Blue-green Algae**

| Test species | Effect/ parameter | Time (d) | NOEC (mg/l) | Reference |
|---|---|---|---|---|
| | **Growth inhibition** | | | |
| *Scenedesmus quadricauda* | $EC_3$ | 8 | 9.3 | Bringmann and Kühn, 1977 |
| *Selenastrum capricornutum* | $EC_{50}$ | 4 | 5.5 | Forbis, 1990 |
| *Microcystis aeruginosa* | $EC_3$ | 8 | 1.3 | Bringmann and Kühn, 1978a,b |

## 6.3 TERRESTRIAL ORGANISMS

An acute oral toxicity > 103 mg/kgbw was reported for Redwinged Blackbirds after an 18 hour exposure. Due to the repellency of BA to birds, there is no potential for acute avian poisoning (Schafer *et al*, 1983).

## 6.4 EVALUATION

The acute toxicity of BA to aquatic organisms is > 1 mg/l, it is readily biodegradable and does not bioaccumulate. Thus BA need not be classified as dangerous to the environment according to the 7th amendment of Council Directive 67/548/EEC.

Because of its distribution into the environment and biodegradability in aquatic systems, toxic concentrations of BA are unlikely to occur in water during normal use.

# SECTION 7. KINETICS AND METABOLISM

## 7.1 HUMAN

No data are available.

## 7.2 EXPERIMENTAL

### 7.2.1 *In Vivo* Studies

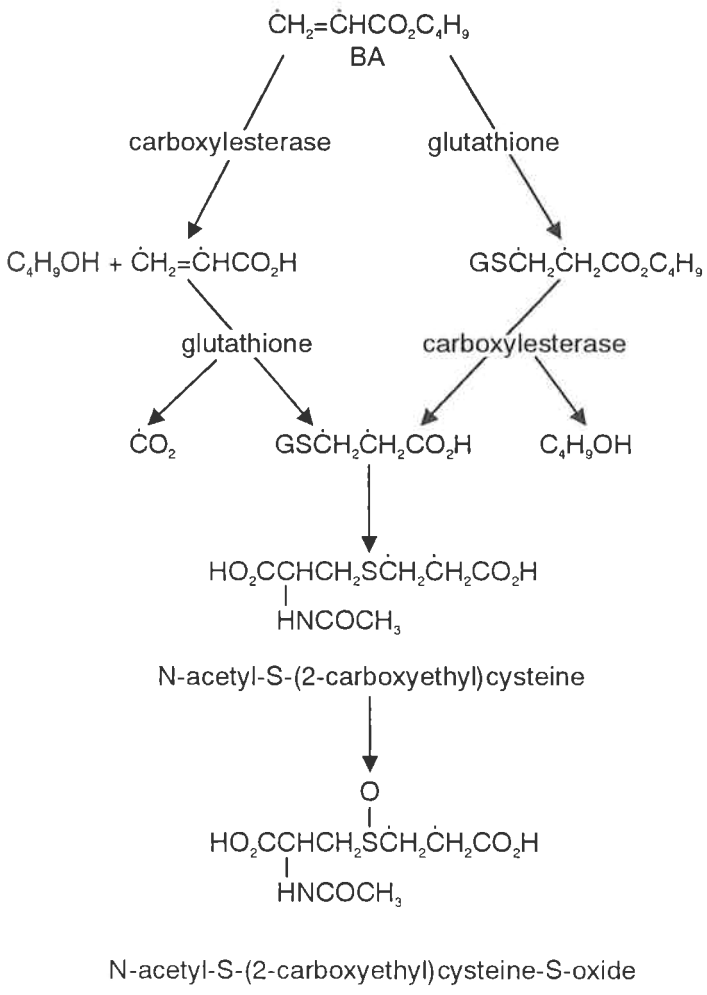
The metabolism and disposition of radiolabelled BA, butyl (2,3-$^{14}$C)acrylate, in male F344 and male Wistar rats have been studied by oral gavage, by i.v. and i.p. administration, and by inhalation.

After oral administration of $^{14}$C-labelled BA (4, 40 and 400 mg/kgbw) to male F344 rats, it was rapidly absorbed from the gastrointestinal tract and quickly metabolised. No parent compound was detected in any urine, bile or tissue extract examined. The majority (75%) of radioactivity was exhaled as $^{14}CO_2$ within 24 hours. Respective elimination in urine and faeces accounted for approximately 10% and 2% of the dose. Two major metabolites in urine were identified as N-acetyl-S-(2-carboxyethyl)cysteine and N-acetyl-S-(2-carboxy-ethyl)cysteine-S-oxide. Gastrointestinal absorption and metabolism were largely unaffected by dose in the range studied. Some minor saturation was observed at 400 mg BA/kgbw, as evidenced by the appearance of chromatography of 3 minor urinary peaks, one of these peaks was tentatively identified as acrylic acid (Sanders *et al*, 1988).

Similar results were obtained in male Wistar rats after oral and i.p. administration of $^{14}$C-BA (100 mg/kgbw) (Sapota and Jakubowski, 1990; Sapota, 1991). The half-life in plasma after oral administration was 24 hours. After i.p. administration the loss of $^{14}$C in plasma was biphasic. The first fast phase ($t_{½}$ = 1.7 h) correlated with the exhaled $^{14}CO_2$, followed by a slow phase ($t_{½}$ = 44 h). At 48 hours after oral and i.p. administration almost 100% of $^{14}$C had been eliminated and hence only small amounts of radioactivity were found in various tissues. Initially, the highest concentrations were found in liver, kidneys and lungs 2 hours after oral and 0.5 hours after i.p. administration of BA. After remaining constant for several hours, $^{14}$C levels decreased substantially between 24 and 48 hours after administration in all tissues except erythrocytes, adipose tissue and sciatic nerve (Sapota and Jakubowski, 1990; Sapota, 1991).

After i.v. administration of $^{14}$C-BA (40 mg/kgbw) to male F344 rats, radioactivity derived from BA was rapidly distributed to all major organs examined. Elimination of the radioactivity from the organs and tissues was biphasic. A rapid elimination phase was observed for the first 2 hours after dosing, followed by a slow elimination phase which persisted until the end of the study (at 70 hours). An exception to this pattern was adipose tissue where the concentration increased during the first 24 hours. These results probably represent the incorporation of radiolabelled acetyl coenzyme A (acetyl-SCoA) into *de novo* synthetised lipids, proteins, and other biochemical intermediates. The amount of radioactivity in the blood was greater after i.v. than after oral administration. More than 55% of the radioactivity found in blood after 24 hours was 'covalently bound' to the membranes of erythrocytes. Approximately 45% of the radioactivity was exhaled as $^{14}CO_2$ within 24 hours, whilst 15% and 1.2% were excreted in urine and faeces respectively (Sanders *et al*, 1988). The proposed metabolic pathway for BA is shown in Figure 1.

**Figure 1 Metabolic Pathway in Rats** (after Sanders *et al*, 1988)



In a recent paper, Linhart *et al* (1994) confirmed the presence of the urinary mercapturate and its S-oxide and reported the identification of 3-hydroxypropionate, citrate and isocitrate. These findings further support the hypothesis that the released acrylic acid is metabolised by the propionate pathway. The authors found no metabolites consistent with the metabolic activation of BA to 1-butyloxiranecarboxylate and subsequent hydrolysis or reaction with glutathione (GSH).

Administration of 90 mg BA/kgbw (0.7 nmol/kgbw) to Wistar rats by the i.p. route, resulted in excretion of 6% of the administered dose as mercapturic acids in the urine within 24 h. Inhibition of carboxyl esterases with tri-*o*-tolyl phosphate (TOTP) increased the mercapturic acid excretion from 6% to 38% (Delbressine *et al*, 1981). Similar findings were reported by Kopecky *et al* (1985).

Svetlakov *et al* (1989) reported covalent binding of BA to plasma proteins after i.p. administration to rats.

Vodička *et al* (1990) studied the effect of inhaled BA (0, 1,000, 2,000 and 4,000 mg/m$^3$ for 6 h) on tissue total (T-SH) and non-protein (NBH) SH-groups and urinary thioether excretion of male Wistar rats. While the total amount of thioethers excreted in urine increased with the administered concentration, the proportion of the dose excreted as thioether conjugates remained constant at 2.2-2.6 %. The concentration of BA in the inhaled air which caused a 50% reduction in NBH after a 6 hours exposure was estimated as, blood 68.6 m mol/m$^3$, liver 39.4 mmol/m$^3$ lungs 104.1 mmol/m$^3$ and brain 140.2 mmol/m$^3$.

### 7.2.2 *In Vitro* Studies

The rate of butanol formation by hydrolysis of BA catalysed carboxylase obtained from rat liver microsomes was 4 times greater than methanol formation by hydrolysis of methyl acrylate and methyl methacrylate in the same *in vitro* system (Kotlovsky *et al*, 1988).

Non-enzymatic reaction of BA with GSH (5 mM) resulted in a half-life of 16 minutes as determined by the depletion of free SH-groups (Vodička *et al*, 1990).

The half-life of BA in rat blood was 7.7 minutes following the addition of 1 μmol/ml BA. Only small amounts of acrylic acid, far lower than the corresponding amount of BA, were found after 20 minutes. As in the case of methyl and ethyl acrylates, binding to sulphydryl groups may play a role in the degradation of BA in blood. When BA was incubated with rat liver, kidney or lung homogenates *in vitro*, it was hydrolysed by non-specific carboxylesterases to acrylic acid and *n*-butanol. Similar rates of hydrolysis have been reported for methyl and ethyl acrylate with liver,

kidney, and lung homogenates. Degradation occurred more rapidly in the liver homogenate than in blood (Miller *et al*, 1981).

These findings were corroborated by Wiegand (1990), who compared the *in vitro* metabolism of BA in tissues from different species (rat, mouse, guinea pig, rabbit and man). In blood, the respective half-lives for BA were found to be 3.7, 4.3, 1.6, 2.3 and 37.6 minutes for rat, mouse, rabbit, guinea pig and man respectively. Further analysis revealed that in rat and mouse plasma, BA was rapidly hydrolysed by alkyl ester specific carboxylesterases ($t_{½}$ = 2.0-13.4 min), whereas human plasma does not contain these enzymes. Only minor hydrolysing activity was observed in human blood ($t_{½}$ = 89.3 min), probably due to the action of butyryl cholinesterase. In suspensions of erythrocytes $t_{½}$ was 4.5, 10.0, 8.9, 5.0 and 29.9 minutes for rat, mouse, guinea pig, rabbit and man respectively. In the liver, all species exhibited high carboxylesterase activity without major species differences. Based on the above, the author concluded that following inhalation exposure to BA, a higher steady-state blood concentration may be attained in man (Wiegand, 1990). These *in vitro* studies cannot really provide much quantitative information on tissue concentrations in human beings or animals (Frederick, 1993).

*In vitro* studies of the nasal mucosa of $B6C3F_1$/CreBR mice, were used to determine the ratio $V_{max}/K_m$ (unsaturated state, first order kinetics). It was demonstrated that BA was hydrolysed by carboxylesterase in the nasal mucosa to a greater extent than methyl or ethyl acrylate. At saturated substrate concentrations, both ethyl and methyl acrylate were hydrolysed to a greater extent than BA. From these *in vitro* studies, it was suggested that extensive hydrolysis of BA would occur in the nasal mucosa in exposed animals, yielding acid metabolites which are capable of producing lesions in the olfactory epithelium (Stott and McKenna, 1985).

## 7.3 SUMMARY

BA is rapidly absorbed following oral and inhalation exposure. Disposition of BA, as judged by the distribution of radio-activity, is rapid and widespread throughout the body following oral, i.v. and i.p. exposure.

In common with other simple acrylate esters there are 2 basic metabolic pathways, both are detoxifying. The primary result is carboxylesterase hydrolysis of the ester bond, resulting in the formation of acrylic acid and *n*-butanol, both of which are further metabolised to $CO_2$. There is no evidence for the formation of an epoxide during the metabolism of BA.

The secondary route is conjugation with glutathione which occurs either spontaneously (Michael addition) or catalysed by glutathione transferases. The mercapturic acids and derivatives are rapidly excreted in the urine.

# SECTION 8. EFFECTS ON EXPERIMENTAL ANIMALS AND *IN VITRO* TEST SYSTEMS

## 8.1 ACUTE TOXICITY

### 8.1.1 Oral

Acute oral $LD_{50}$ values are detailed in Table 10.

**Table 10 Acute Oral Toxicity**

| Species | $LD_{50}$ (g/kgbw) | Reference |
|---|---|---|
| Mouse | 5.4 | Tschernikowa *et al*, 1979 |
| Mouse | 7.6[1] | Tanii and Hashimoto, 1982 |
| Rat | 3.7 | Smyth *et al*, 1951 |
| Rat | 9.1 | Carpenter *et al*, 1974 |
| Rat | 6.2 | Tschernikowa *et al*, 1979 |
| Rat, ♂<br>Rat, ♀ | 6.2<br>4.9 | Vernot *et al*, 1977 |
| Rat | 3.2 (approximately)[2] | Oettel and Hofmann, 1958 |
| Rabbit | 1.8 (approximately)[2] | Oettel and Hofmann, 1960a,b |

1 58.98 mmol/kgbw
2 Only 2 animals used

The published oral $LD_{50}$ values for BA following administration to mice, rats and rabbits are detailed in Table 10. The only publications which report clinical observations are those of Oettel and Hofmann (1958, 1960a) which show that oral administration of BA to rats and rabbits produced diarrhoea, reduced bodyweight gain and thickening of the gastric mucosa with diffuse or local erythema in the presence and absence of haemorrhage.

### 8.1.2 Dermal

A number of investigators have reported acute lethal doses for BA administered dermally to rabbits and rats (Table 11).

**Table 11 Acute Dermal Toxicity**

| Species | $LD_{50}$ (g/kgbw) | Reference |
|---|---|---|
| Rat | 1.7[2] | Sokal *et al*, 1980 |
| Rabbit | 3.1[1] | Smyth *et al*, 1951; Fassett, 1963 |
| Rabbit | 2.0 | Carpenter *et al*, 1974 |
| Rabbit | 5.7 | Vernot *et al*, 1977 |
| Rabbit | 1.7[2] | Sokal *et al*, 1980 |

1 3.4 ml/kgbw
2 Lowest lethal dose

### 8.1.3 Inhalation

Acute inhalation $LD_{50}$ values are detailed in Table 12.

**Table 12 Acute Inhalation Toxicity**

| Species | Time (h) | $LC_{50}$ (ppm) | Reference |
|---|---|---|---|
| Rat | Not specified | 2,595[2] | Tschernikowa *et al*, 1979 |
| Rat[1] | 4 | 2,540 | Zeller and Klimisch, 1979 |
| Rat | 4 | 1,970 | Hofmann and Klimisch, 1980 |
| Rat | 4 | 2,730[3] | Oberly and Tansy, 1985 |
| Mouse[1] | 4 | 1,380 | Zeller and Klimisch, 1979 |
| Mouse | 4 | 1,290 | Zeller and Klimisch, 1979 |
| Chinese hamster[1] | 4 | 1,681 | Zeller and Klimisch, 1979 |
| Chinese hamster[1] | 4 | 1,220 | Zeller and Klimisch, 1979 |

1 The $LC_{50}$ values are in the same range for animals fasted before exposure or for non-fasted animals
2 13.8 mg/l
3 Confidence limits at 95% were 2,430-3,067 ppm

Clinical signs exhibited by rats on the day of exposure included increased ocular and nasal discharge (sanguineous in some cases), agitation, dyspnoea, hyperaemia of the nasal and ocular mucosa, pulmonary haemorrhages, pulmonary oedema, and emphysema (Tschernikowa *et al*, 1979; Zeller and Klimisch, 1979; Hofmann and Klimisch, 1980). Animals that died exhibited

discoloration of the lungs and liver at necropsy. Those that survived the 14 day observation period showed no macroscopic lesions (Nachreiner and Dodd, 1989).

Variability of the $LC_{50}$ values (Table 12) may be the result either of using nominal rather than analytically determined concentrations, or of using different strains of animals or different experimental conditions (nose only or whole body) and possibly the use of samples of different grades of purity.

Data for lethality, not adequate for calculating $LC_{50}$ values, are shown in Table 13.

**Table 13 Acute Inhalation Lethality Data**

| Species | Time (h) | Concentration (ppm) | Deaths/animals used | Reference |
|---|---|---|---|---|
| Rat | 1 | 4,398 | 3/10 | Nachreiner and Dodd, 1989 |
| Rat, ♂ | 1 | 6,360 | 2/5 | Vernot *et al*, 1977 |
| Rat, ♀ | 1 | 5,100 | 4/5 | |
| Rat | 4 | 1,000 | 1/6 | Carpenter *et al*, 1974 |
| Rat | 4 | 1,000 | 5/6 | Smyth *et al*, 1951; Fassett, 1963 |

Nachreiner and Dodd (1989) reported clinical observations in male and female rats during and after inhalation exposure to BA; these included blepharospasm, lacrimation, perinasal and perioral wetness and erythema of the paws during exposure, blepharospasm on removal from exposure and mouth breathing, perinasal and periocular encrustation and unkempt fur for 4 days after exposure.

### 8.1.4 Summary

Acute toxicity studies in experimental animals have shown that BA is of low oral and dermal toxicity, and to be moderately toxic via the inhalation route.

## 8.2 SKIN, RESPIRATORY TRACT AND EYE IRRITATION, SENSITISATION

### 8.2.1 Skin Irritation

Dermal exposure of various laboratory animals elicited a wide range of irritation responses depending upon the duration and frequency of contact. Unoccluded application of 10 µl undiluted

BA to the shaved dorsal skin of 1 albino rabbit for 24 hours resulted in mild to severe capillary injection without the formation of oedema (Smyth *et al*, 1951; Carpenter *et al*, 1974).

Signs of local inflammation were seen after exposure to undiluted BA, with occluded application to rabbits. Erythema, mild oedema and desquamation of the surface skin layer occurred after brief treatments of 1, 5 and 15 minutes. Allowing the occluded undiluted BA to remain on the skin for 20 hours caused a definite to very severe erythema and oedema. In concurrent studies with methyl and ethyl acrylates, it was shown that the degree of irritation caused by BA was less severe than that caused by the other two esters (Oettel and Zeller, 1958; Gelbke, 1978).

No information on clinical observations is given in any of the references quoted above.

### 8.2.2 Respiratory Tract Irritation

In acute inhalation studies, a number of clinical signs were seen in fasted or non-fasted animals (rats, mice, guinea pigs) exposed to $LC_{50}$ concentrations (Table 12). The most common signs, in all species, were ocular and nasal discharge, pulmonary hyperaemia and dyspnoea. Non-fasted Chinese hamsters also developed cardiac dilation, probably as a consequence of lung irritation (Zeller and Klimisch, 1979).

In a sub-chronic study using Sprague-Dawley rats, 20 male and 20 female animals were exposed to BA at concentrations of 21, 108, 211 and 546 ppm. Exposures were conducted for 6 h/d, 5 d/wk for 13 weeks. Between the 3rd and 13th weeks, 31 of the 40 animals exposed to 546 ppm died. These rats exhibited sanguineous ocular and nasal discharges, rhinitis, hyperaemic nasal mucosa, oedematous nasal epithelium, metaplasia of the olfactory epithelium, and extensive and advanced necrosis of the lungs associated with gram positive bacteria. Cornification of the epithelium of the trachea and bronchi, pulmonary hyperaemia and pneumonia were also reported at this dose. At 211 ppm all the animals survived but irritation occurred in both the ocular and nasal mucosa along with atrophy of both the olfactory mucosa and Bowman's glands. Only minor effects occurred in the nasal mucosa with exposure to 108 ppm; at 21 ppm no toxic effects were noted (Klimisch *et al*, 1978).

Exposure of rats to 13 mg/l (2,598 ppm) BA for an unspecified time resulted in hyperaemia of nasal mucosa, eyes and the skin of the ears and paws (Tschernikova *et al*, 1979). The same authors also reported that similar signs were exhibited by mice exposed to air concentrations > 5,750 ppm, again without specifying the exposure time.

Oberly and Tansy (1985) reported that Sprague-Dawley rats exposed to BA vapour ranging from 1,990 to 3,041 ppm (4 hours, observation period 24 hours) demonstrated irritation of the eyes, nose, and respiratory tract. Laboured breathing occurred for at least some of the exposure period.

### 8.2.3 Gastrointestinal Tract Irritation

Oettel and Hofmann (1958; 1960a) administered solutions of BA (10-20%) in water and gum tragacanth to rats by gavage. The macroscopic pathological examination revealed gastric perforation in several animals.

Administration of a single dose of 520 mg/kgbw BA by gavage in corn oil to male F344 rats did not produce gastric oedema. When the same dose was administered in water, gastric oedema occurred. Comparison with other acrylic esters showed that methyl and ethyl acrylates produce a more severe gastric irritation in rats than BA or acrylic acid. In the rat, the forestomach is more prone to the irritating effects of acrylic esters than the glandular stomach (Ghanayem *et al*, 1985).

### 8.2.4 Eye Irritation

Eye irritation can result from liquid or vapour contact and may consist of tissue damage and/or sensory effects. Undiluted BA applied to the eyes of rabbits, in amounts of 0.05 ml and 0.1 ml, caused the production of small opacous plaques on the cornea which could only be seen with the use of fluorescein (Smyth *et al*, 1951; Oettel and Zeller, 1958; Carpenter *et al*, 1974). The mucosal damage decreased in severity within 24 hours (Oettel and Zeller, 1958).

In a 2-year rat inhalation study, 30% of the animals in the high exposure group (135 ppm) showed evidence of corneal stippling, parenchymal degeneration and parenchymal neovascularisation. Other exposure groups were comparable to controls. During a 6 month recovery period, a partial regression of the corneal neovasularisation was observed (Reininghaus *et al*, 1991).

### 8.2.5 Sensitisation

Studies with guinea pigs using a variety of protocols (Pollack method, Split Adjuvant technique, Magnusson and Kligman assay, epicutaneous methods and intradermal maximisation test) have shown that dermal exposure to BA and other acrylates causes a delayed contact hypersensitivity. Cross-sensitisation to other monoacrylates and diacrylates may occur (Draize *et al*, 1944; Levine, 1960; Magnusson and Kligman, 1970; Maguire and Chase, 1972; Parker and Turk, 1977, 1983; Van der Walle *et al*, 1982a,b).

### 8.2.6 Summary

BA is irritant to the skin, gastrointestinal tract and respiratory tracts. BA can cause skin sensitisation in susceptible animals. BA may cross-react with other acrylic acid esters.

## 8.3 SUBCHRONIC TOXICITY

### 8.3.1 Oral

*Gavage*

Three rabbits (strain not specified) received 1 ml/kgbw (equivalent to 898 mg BA/kgbw) applied 9 times over a 2 week period as a 10% aqueous emulsion in tragacanth via stomach tube. No signs of intoxication were observed other than a transient lack of appetite, tachypnoea and mild diarrhoea. The substance was tolerated with no evidence of liver (Bromsulphalein) and kidney (blood urea nitrogen) disfunction and with no haematological changes in the blood count (Hb, red and white cells). Necropsy yielded no treatment related pathological findings (Oettel and Hofmann, 1960b).

A group of male and female rats (group size not specified) was dosed with 150 mg BA/kgbw/d for 13 weeks by gavage. All rats showed increased relative liver weights. No histopathological changes were observed (Gorzinski *et al*, 1982).

*Drinking Water*

Groups of male and female rats were given BA in their drinking water at concentrations equivalent to 0, 12, 73 or 84 mg/kgbw/d for males and 0, 15, 91 or 111 mg/kgbw/d for females, for 13 weeks. Water consumption was slightly reduced at all dose levels. Decreased body weight gain was observed in males receiving 84 mg/kgbw/d. No histological changes were observed in the tissues (Gorzinski *et al*, 1982).

### 8.3.2 Dermal

In a 2-week test the dermal toxicity of BA was studied in 5 male C3H/HeJ mice per group with cutaneous application of 25 µl/d of 1% BA in acetone for 10 days. Neither irritation nor fatalities were observed. By contrast, concentrations of 5, 10, 50, and 100% BA produced skin irritation using the Draize procedure (Peterson, 1979).

### 8.3.3 Inhalation

In a 13-week inhalation study, Sprague-Dawley rats were exposed to 0, 21, 108, 211 and 546 ppm (6 h/d, 5 d/wk, 20 male and 20 female rats per concentration). At 546 ppm, 31 out of 40 animals died between weeks 3 and 13. No mortalities were observed in the 3 lowest dose groups. Bloody ocular and nasal discharges and a significantly lower body weight gain were observed in the 546 and 211 ppm groups. Hyperaemic nasal mucosa, oedematous epithelium and frequently extensive and advanced necrosis of the lungs associated with gram positive bacteria were observed histologically; metaplastic changes of the olfactory epithelium and in the epithelium of the trachea and bronchi (cornification) as well as pulmonary hyperaemia and pneumonia also occurred in the 546 ppm group. At 211 ppm, BA produced only slight oedema and erosion of the nasal mucosa in a few individuals of this group. The relative liver weights in female rats were dose-dependently elevated whereas only the thyroid, adrenal and lung weights were increased in the 546 ppm group. Exposure to the 108 ppm concentration led to relatively minor influences of the test substance (body weight gain, relative liver weight) but no histopathological changes were observed (Klimisch et al, 1978). The NOEL in this study was 21 ppm.

### 8.3.4 Summary

Following prolonged or repeated exposure, the most common effects observed are those associated with the irritating properties of BA. No unusual systemic toxic effects have been reported.

## 8.4 GENETIC TOXICITY

*In vitro* genetic toxicity assays are used routinely as the first screen for assessing the genotoxic activity of chemicals. These assays, however, provide information only on the intrinsic potential of these chemicals to cause damage to the DNA. To determine whether or not this intrinsic potential is expressed in the whole animal it is necessary to conduct *in vivo* genetic toxicity assays which take into account absorption, distribution, metabolism and excretion of the test material. The results of *in vivo* assays are more relevant to human hazard.

### 8.4.1 *In Vitro* Gene Mutation in Bacteria

BA has been reported as non-mutagenic in several *in vitro* bacterial gene mutation assays. Oesch (1977) tested BA in a plate incorporation assay at concentrations of 2.8-900 μg/plate using *Salmonella typhimurium* strains TA1535, TA1537, TA98 and TA100 in the presence or absence of an auxiliary metabolic activation system (rat liver S9-mix). No mutagenic or bacteriotoxic effect was

observed. Based on the hypothesis that BA may be metabolised via an epoxide metabolite, BA was retested in *Salmonella typhimurium* strain TA98 in the presence of an epoxide hydrolase inhibitor, 1,1,1-trichloropropene-2,3-oxide. No mutagenic effect was observed (Oesch, 1977).

Waegemaekers and Bensinck (1984) tested BA in the presence and absence of both Aroclor 1254 and phenobarbital-induced rat liver S9-mix using the *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100. Concentrations of 30-2,000 μg/plate were tested in a standard plate incorporation assay whereas concentrations of 15-1,500 μg/plate were tested in a liquid preincubation assay using Aroclor 1254 induced S9 and strain TA100. BA was prevented from evaporating during the treatment period. No mutagenic effect was observed in any of the strains tested.

Similarly, Zeiger *et al* (1987) report BA as non-mutagenic in a pre-incubation assay using *Salmonella typhimurium* strains TA100, TA1535, TA1537 (or TA97) and TA98 in the presence or absence of Aroclor 1254 induced rat and Syrian hamster S9-mix, when tested at a range of concentrations between 3.3 and 10,000 μg/plate.

McCarthy (1984), citing both BASF and US-NTP results, reported BA as non-mutagenic in the Ames test but no supporting data were provided.

### 8.4.2 *In Vitro* Gene Mutation in Mammalian Cells

No data are available.

### 8.4.3 *In Vitro* Chromosome Aberrations

Wiegand *et al* (1989) tested BA in an *in vitro* micronucleus assay using Syrian Hamster Embryo (SHE) fibroblasts. BA was reported as non-clastogenic when tested up to 10 μg/ml in the absence of S9-mix; SHE cells are reported to possess intrinsic metabolic capacity. However no measure of cytotoxicity was provided in the data and so the top concentration tested may not have been high enough to provide an adequate test.

BA was reported to induce chromosomal aberrations following treatment of Chinese Hamster Ovary (CHO) cells in the absence of metabolic activation, but these increases in aberrant cells were observed only at excessively cytotoxic concentrations of BA (US-NTP, 1991) and therefore these increases are considered to be of no biological significance. In the presence of metabolic activation, small increases in the incidence of chromosomal aberrations were reported but these

increases were generally less than twice the concurrent control value and were not concentration-related (US-NTP, 1991). The biological significance of such increases is therefore questionable.

### 8.4.4 Other *In Vitro* Genotoxic Endpoints

BA was reported to induce small increases in the frequency of sister chromatid exchanges (SCEs) following treatment of Chinese Hamster Ovary (CHO) cells (US-NTP, 1991). The increases were generally less than twice the concurrent control values and the biological significance of such increases is therefore questionable.

Wiegand *et al* (1989) tested BA in *in vitro* UDS and cell transformation assays in the SHE cells detailed in Section 8.4.3. Although both assays showed no genotoxic activity of BA, they were conducted to inadequate protocols and add little to our knowledge of the genotoxicity of BA.

### 8.4.5 *In Vivo* Chromosome Damage Assays

Engelhardt and Klimisch (1983) tested BA in an *in vivo* chromosomal aberration assay using rats and Chinese hamsters. Male and female animals were exposed to BA via inhalation at concentrations of 817 ppm (Chinese hamsters) or 820 ppm (rats), 6 h/d for 4 consecutive days. A positive control was not included in the assay. Significant adverse reactions were observed at these concentrations in both species and included dyspoena, disequilibrium and bloody discharge from the eyes and nose. In addition, 4 of the 10 Chinese hamsters died following exposure. The surviving animals were killed 5 hours after the end of the 4th exposure and 100 metaphases per animal from bone marrow preparations were analysed for chromosomal damage. No depression in mitotic activity or increase in chromosomal aberrations were observed in the BA treated hamsters or rats indicating that BA is non-clastogenic *in vivo* when tested up to the Maximum Tolerated Dose based on lethality.

### 8.4.6 *In Vivo* DNA-Binding

No data are available.

### 8.4.7 Evaluation of Genotoxicity

BA shows no evidence of *in vitro* or *in vivo* genotoxicity in the assays.

## 8.5 CHRONIC TOXICITY AND CARCINOGENICITY

### 8.5.1 Oral

No data are available.

### 8.5.2 Dermal

Forty male C3H/HeJ mice were exposed to topical applications of 25 µl of a 1% solution of BA in acetone (approximately 0.2 mg BA/mouse/application). Applications were performed 3x/week for the entire lifespan of the mice. Control groups were exposed to acetone alone or to 0.1% 3-methylcholanthrene in acetone (positive control). Mice exposed to BA survived an average 503 days compared to 484 days for the control group. Early deaths due to tumour development occurred in the positive control group. Necropsy included the histological examination of all dorsal skin and all lesions. In the BA group, no treatment-related tumours were found. Thirty-nine of 40 mice exposed to 3-methylcholanthrene developed skin tumours, the majority of which were squamous cell carcinomas (De Pass *et al*, 1984).

### 8.5.3 Inhalation

In a 2-year inhalation study with a 6-month recovery sub-group, 86 male and 86 female Sprague-Dawley rats (35 day old at the start of the study) were exposed during the first 3 weeks to 0, 5, 15 and 45 ppm and thereafter to 0, 15, 45 and 135 ppm BA. The exposure regime was 6 h/d, 5 d/wk for 24 months. After 12, 18, and 24 months, 10 or 15 male and female rats per treatment group were killed for interim examination. All rats that had died or were killed were subjected to necropsy and organ weights were determined. Clinical signs, mortality, food consumption, body weight gain, and results of blood tests in the exposed animals were similar to control. Lower weights (5-17%) were recorded for kidneys, thyroid, heart and liver in some of the exposed rats. These were not considered to be of toxicological significance due to inconsistent dose-dependence and lack of correlation with histological changes. Centrally localised or diffused stippling of the corneal epithelium and cloudiness of the corneal parenchyma with various degrees of neovascularisation was observed in animals exposed to 135 ppm. The effects were similar in male and female rats and increased with the length of exposure and concentration. Within the nasal mucosa of all exposed animals, atrophy of the neurogenic epithelial cells and hyperplasia of reserve cells was observed. The changes were dose-related and mainly affected the anterior part of the olfactory epithelium. Both corneal and olfactory epithelial effects were attributed to the irritancy of BA. In the 6 month recovery groups, reconstructive effects such as replacement of altered olfactory and

respiratory epithelium, and partial regression of corneal neo-vascularisation was observed. A full analysis of all neoplastic lesions showed a heterogeneous spontaneous tumour distribution unrelated to treatment. The incidence of sarcomas varied significantly in all tissues or sites, but exhibited no dose-dependency. Similarly, the incidence of all malignant mesenchymal tumours (mainly soft tissue sarcomas) did not indicate an exposure-related tumour increase. In summary, there was no evidence of chronic systemic toxicity or a carcinogenic effect of BA under these experimental conditions (Reininghaus *et al*, 1991).

### 8.5.4 Summary

Chronic inhalation and dermal assays with BA showed no evidence of chronic systemic toxicity nor of carcinogenic potential.

## 8.6 REPRODUCTIVE TOXICITY, EMBRYOTOXICITY AND TERATOGENICITY

### 8.6.1 Oral

Marks and Jones-Prince (1982) administered BA, dissolved in cotton-seed oil, to pregnant CD1 mice using doses of 0, 100, 1,000, 2,000, 2,500, 3,000 and 4,000 mg/kgbw by oral gavage (stomach tube) daily from day 6 to 15 post coitum. The dose of 4,000 mg/kgbw was lethal for all pregnant dams; 2 of 30 died at 3,000 and 2,500 mg/kgbw, 1 of 29 at 2,000 mg/kgbw, 1 of 27 at 1,500 mg/kgbw, and 1 of 30 animals at 1,000 mg/kgbw. All animals survived the 100 mg/kgbw dose level. Maternal toxicity was noted at dose levels of > 1,500 mg/kgbw in the form of a slower body weight gain although at 1,000 mg/kgbw a significant increase in relative maternal liver weight was observed. Embryolethality and embryotoxicity (cleft palates exencephaly, open eyes, fused arches, fused ribs) were observed at 2,500 mg/kgbw and higher doses. Embryotoxic, but not embryolethal, effects were noted at 1,000, 1,500 and 2,000 mg/kgbw. No evidence of maternal toxicity, embryolethality or embryotoxic effects was found in the 100 mg/kgbw group (NOEL). The authors considered that the increase in maternal liver weight observed at 1,000 mg/kgbw did not reflect maternal toxicity and concluded that the embryotoxic effects seen at this dose level constitute a true teratogenic effect.

### 8.6.2 Inhalation

Groups of pregnant rats were exposed to atmospheres containing, nominally, 0, 25, 135 and 250 ppm BA, for 6 h/d, on days 6 to 15 of gestation. Signs of maternal toxicity were observed only in animals exposed to 135 or 250 ppm and consisted of nasal and ocular discharges and a

statistically significant reduction in body weight gain. Increases in post-implantation losses and an apparent dose related decrease in the number of live foetuses were also reported at these vapour concentrations, although only the former were statistically significant. There was no evidence of retarded foetal growth or increases in the incidence of skeletal or soft tissue abnormalities. At 25 ppm, neither maternal toxicity nor embryolethality occurred. BA was not teratogenic under the conditions of this assay (Merkle and Klimisch, 1983).

### 8.6.3 Summary

By inhalation, BA was maternally toxic and embryotoxic in rats at concentrations of 135 ppm and above. The NOEL was 25 ppm. By the oral route, BA was maternally toxic and embryotoxic in mice at 1,000 mg/kgbw/d and above. The NOEL of 100 mg/kgbw/d. It is concluded that, at the currently accepted occupational exposure levels, BA represents no reproductive risk to man.

# SECTION 9. EFFECTS ON HUMANS

## 9.1 SKIN IRRITATION AND SENSITISATION

In a study to investigate the cause of dermatitis in dental workers, 46 subjects were patch tested with BA (0.5 or 1.0% in petrolatum). One subject gave an allergic response, whilst 11 others showed signs of irritation (Kanerva *et al*, 1988). BA has also been shown to cross react in patients sensitised to ethylhexyl acrylate and *n*-tert-butylmaleic acid monoamide (Jordan, 1975).

A case of skin sensitisation, manifest by eczema on the bridge of the nose and attributed to BA in spectacle frames, was reported by Hambly and Wilkinson (1979).

## 9.2 CHRONIC TOXICITY

Thirty three workers (20 women and 13 men) were exposed for 5 years during developmental research to an atmosphere containing concentrations of up to 50 mg/m$^3$ (9.4 ppm) of BA, 4-58 mg/m$^3$ (1-14 ppm) of ethyl acrylate and 0.11-2 mg/m$^3$ (0.05-0.9 ppm) of acrylonitrile. The clinical and laboratory investigations diagnosed disturbances of the autonomous nervous system and 'neurotic' disturbances in 14 individuals which were 'functional in nature as indicated by corresponding EEG recordings' (Kuželová *et al*, 1981). Because of mixed exposures and in the absence of further data it is impossible to evaluate this study.

## 9.3 SUMMARY

With the exception of evidence that BA may give rise to skin sensitisation in human beings, there are no relevant data available.

# SECTION 10. FIRST AID AND SAFE HANDLING ADVICE

## 10.1 FIRST AID AND MEDICAL TREATMENT

There is no specific treatment or antidote for over-exposure to BA. Supportive medical treatment as indicated by the patient's condition is recommended.

### 10.1.1 Skin and Eye Injuries

Clothing contaminated with BA should be removed. Affected areas of skin must be washed with copious quantities of water. The skin must be rinsed for at least 10 minutes. If the eyes are splashed, they should be irrigated immediately with eye-wash solution or clean water, holding the eyelids apart for at least 10 minutes. A physician should then be consulted.

### 10.1.2 Inhalation

The patient must be taken into fresh air, kept warm and at rest if he experiences difficulty in breathing after inhaling BA fumes. If the patient stops breathing, artificial respiration should be administered until qualified medical personnel is able to take over. Medical aid should be summoned immediately.

### 10.1.3 Ingestion

If BA has been swallowed, do not induce vomiting. Never give anything by mouth to an unconscious person. A physician should be consulted immediately.

## 10.2 SAFE HANDLING

### 10.2.1 Safety at Work

The main risk of injury stems from BA's irritating action on the skin and mucous membranes. Contact with the skin and eyes should therefore be avoided as should inhalation of high concentrations of BA vapour. BA should be used only in well ventilated areas. BA vapour is denser than air; pits and confined spaces should be avoided.

Suitable respiratory equipment must be worn on occasions when exposure to BA vapour above the recommended exposure limit is likely.

The following protective clothing must be worn when handling BA: eye-face protection and rubber gloves (preferably nitrile) which should be changed regularly to avoid permeation. Rubber boots should also be worn when handling large quantities.

### 10.2.2 Storage Safety

BA is stable in the presence of a polymerisation inhibitor. It is susceptible to polymerisation initiated by prolonged heating or a catalyst. Therefore, the following precautions must always be observed when storing BA:

- BA must be stored under air as the stabiliser (hydroquinone monomethylether) is only effective in the presence of oxygen,
- heat and direct sunlight must be excluded, as these promote polymerisation,
- BA must be stored at temperatures preferably not exceeding 25°C,
- care should be taken to prevent contamination, as contaminants can render the stabiliser ineffective or can react with BA and promote polymerisation.

### 10.2.3 Fire Safety and Extinguishants

BA is classified as a highly flammable liquid. It can form an explosive mixture in air; adequate ventilation should be provided and smoking prohibited. Precautions should be maintained to eliminate all sources of ignition of BA when in contact with air. BA may polymerise on heating. Sealed containers may rupture if hot. Heat, UV-light, peroxide, azo-compounds, alkalis and oxidising agents may cause rapid polymerisation resulting in explosion. Fires can be extinguished with water, alcohol-resistant foam, dry powder or $CO_2$.

If fire does break out, neighbouring tanks and pipelines must be kept cool with plenty of water, otherwise the heat generated by the fire will cause their contents to polymerise.

### 10.2.4 Protection against Fire and Explosion

To avoid ignition, the following precautions are recommended:

- all plant and equipment should be explosion-proof as laid down in national standards,
- all containers must be earthed,
- all sources of ignition must be excluded,
- no smoking is allowed,
- no welding should be done until all tanks and pipelines have been drained and thoroughly flushed with water or hot caustic soda.

## 10.3 MANAGEMENT OF SPILLAGE AND WASTE

In all cases of spillage naked flames should be extinguished. Smoking and sparks must be avoided. Small spills of a few litres can be soaked up with suitable absorbent materials such as sand or earth. BA should not be absorbed onto sawdust or other combustible materials. Larger spills must be prevented from spreading by the use of earth or sand and the material should be pumped into containers.

Surfaces contaminated with BA should be washed well, first with alcohol and then with soap and water. All wastes should be sealed in vapour-tight plastic bags for eventual disposal.

BA should not be allowed to drain into domestic sewers as serious explosion hazards could result. Local authorities should be informed immediately if spilt liquid BA has entered surface water drains.

Waste quantities of BA can be incinerated in accordance with local, state or national regulations. Empty storage drums must be decontaminated before recycling.

When aqueous waste containing BA is discharged to adapted biological waste-water treatment plants it is expected to be mineralised. No disturbance of the bacterial activity of sewage treatment plants is expected if BA is properly diluted.

# BIBLIOGRAPHY

ACGIH (American Congress of Governmental Industrial Hygienists), 1980. *n*-Butyl acrylate. Documentation of the threshold limit values, 4th ed. ACGIH, Cincinatti, OH, 53-54, 173-174.

ACGIH (American Conference of Governmental Industrial Hygienists), 1992. Butyl acrylate. In: Threshold limit values and biological exposure indices for 1992-1993. ACGIH, Cincinatti, OH.

AFS (Arbetarskyddsstyrelsens författningssamling), 1990. Butylakrylat. In: Hygieniska gränsvärden, AFS 1990: 13. AFS, Stockholm.

Amoore JE, Hautala E, 1983. Odor as an aid to chemical safety: odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. J Appl Toxicol 3, 272-290.

Arbeidsinspectie, 1991. De nationale MAC-lijst 1991. Butylakrylaat. DG Arbeid, Ministerie van Sociale Zaken en Werkgelegenheid, Voorburg.

Arbeidstilsynet, 1990. Butylakrylat. In: Administrative normer for forurensning i arbeidsatamosfære, veiledning til arbeidsmiljøloven. Direktoratet for Arbeidstilsynet, Oslo.

Atkinson R, 1987. A structure-activity relationship for the estimation of rate constants for gas-phase reactions of OH radicals with organic compounds. Int J Chem Kinet 19, 799-828.

BASF, 1986. Stoffwerte Butylacrylat. BASF, Ludwigshafen.

BASF, 1988. Bestimmung des Verteilungs-koeffizienten log $P_{ow}$ von *n*-Butylacrylat in 1-Octanol/Wasser bei Raumtemperatur. Analytishes Laboratorium, BASF-ZSZ/AP-M 325 Dokumentation Stoffdaten. BASF, Ludwigshafen, 1-4.

BASF, 1990. Technical information monomers, butyl acrylate: acrylic acid ester for manufacturing polymers and as a feedstock for syntheses. BASF, Ludwigshafen.

BASF, 1991. Biochemical oxygen demand. Personal communication to Dr Scherer, 18.10.1991. BASF, Ludwigshafen, 1-3.

BASF, 1992. Personal communication by W. Druschke, 9 March 1992 [concentrations of BA in working place areas]. BASF, Ludwigshafen.

BASF, 1993. Henrykonstante $H_i$. Stoffdatenservice ZET/FE M 325. BASF, Ludwighshafen.

Belanger PL and Coye MF, 1981. Health hazard evaluation report No. HHE-80-68-871, Sinclair Paint Company, Los Angeles, CA [NTIS PB82-214396]. NIOSH, Cincinnati, OH.

Blum DJW and Speece RE, 1991. Quantitative structure-activity relationships for chemical toxicity to environmental bacteria. Ecotoxicol Environ Safety 22, 198-224.

Bowman JH, 1990. Acute flow-through toxicity of *n*-butyl acrylate to rainbow trout (*Salmo gairdneri*). ABC Labs, Columbia, MI, final report project 37339. BAMM, Washington, DC.

Boxer PA and Reed LD, 1983. Health hazard evaluation report No. HETA-82-051-1269, National Starch and Chemical, Meredosia, IL [NTIS PB84-209923]. NIOSH, Cincinnati, OH.

Bringmann G, 1978. Bestimmung de biologischen Schadwirkung wassergefährndender Stoffe gegen Protozoen I. Bakterienfressende Flagellaten (Modelorganismus: *Entosiphon sulcatum* Stein). Z Wasser- Abwasser-Forsch 11, 210-215.

Bringmann G and Kühn R, 1977. Grenzwerte der Schadwirkung wassergefährdender Stoffe gegen Bakterien (*Pseudomonas putida*) und Grünalgen (*Scenedesmus quadricauda*) im Zellvermehrungs-hemmtest. Z Wasser-Abwasser-Forsch 10, 87-98.

Bringmann G and Kühn R, 1978a. Testing of substances for their toxicity threshold: model organisms *Microcystis (Diplocystis) aeruginosa* and *Scenedesmus quadricauda*. Mitt Internat Verein Limnol 21, 275-284.

Bringmann G and Kühn R, 1978b. Grenzwerte der Schadwirkung wassergefährdender Stoffe gegen Blaualgen (*Microcystis aeruginosa*) und Grünalgen (*Scenedesmus quadricauda*) im Zellvermehrungs-hemmtest. Vom Wasser 50, 45-60.

Bringmann G and Kühn R, 1980. Bestimmung der biologischen Schadwirkung wassergefährhdender Stoffe gegen Protozoen III. Saprozoische Flagellaten. Z Wasser- Abwasser-Forsch 5, 170-173.

Bringmann G and Kühn R, 1981. Vergleich der Wirkung von Schadstoffen auf flagellate sowie ciliate bzw. auf holozoische bakterienfressende sowie saprozoische Protozoen. Gwf-Wasser/Abwasser, 122, 308-313.

Bringmann G and Kühn R, 1982. Ergebnisse der Schadwirkung wassergefährdender Stoffe gegen *Daphnia magna* in einem weiterentwickelten standardisierten Testverfahren. Z Wasser- Abwasser-Forsch 15, 1-6.

Burgess D, 1990. Acute flow-through toxicity of butyl acrylate to *Daphnia magna*. ABC Labs, Columbia, MI. Final report project 37340. BAMM, Washington, DC.

Carpenter CP, Weil CS and Smyth HF, 1974. Range-finding toxicity data, list VIII. Toxicol. Appl. Pharmacol. 28, 313-319.

De Pass LR, Fowler EH, Meckley DR and Weil CS, 1984. Dermal oncogenicity bioassay of acrylic acid, ethyl acrylate and butyl acrylate. J Toxicol Environ Health 14, 115-120.

Delbressine LPC, Seutter-Berlage F and Seutter E, 1981. Identification of urinary mercapturic acids formed from acrylate, methacrylate and crotonate in the rat. Xenobiotica 11, 241-247.

DFG (Deutsche Forschungsgemeinschaft, Senatskommission zur Prüfung gesundheits-schädlicher Arbeitsstoffe), 1992. MAK- und BAT-Werte-Liste 1992, Maximale Arbeitsplatz-konzentrationen und Biologische Arbeitsstoff-toleranzwerte. Mitteilung 28. VCH, Weinheim.

Draize JH, Woodward G and Calvery HO, 1944. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J Pharmacol Exp Ther 82, 377-385.

Džandžannajan AN and Puzjan EA, 1988. [Die bestimmung kleinster Mengen von Butylacrylat und Butylmetacrylayt in der Luft]. Gigiene i Sanitarija 11, 43-45. [Russian]

EEC (European Economic Community), 1992. Commission directive of 30 April 1992 adapting to technical progress for the seventh time Council Directive 67/548/EEC (92/32/EEC). Off J EC, L154, 1-29.

Elf Atochem, 1990. Butyl acrylate. Material safety data sheet. Elf Atochem, Paris la Défense.

Engelhardt G and 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.

Fassett DW, 1963. Esters. In: Patty EA (ed), Industrial hygiene and toxicology, 2nd Rev. vol. 2. New York Interscience, 1877-1880.

Flaherty J, 1989. Personal communication of March 2, 1989 from Keystone Environmental Resources to BCM Labs: $BOD_5$ and COD of ethylacrylate, methyl methacrylate and *n*-butyl acrylate. BCM Labs (Rohm and Haas), Norristown, PA, 1-2.

Forbis AD, 1990. Acute toxicity of *n*-butyl acrylate to *Selenastrum capricornutum* Printz. ABC Labs, Columbia, MI. Final report project 37341. BAMM, Washington, DC.

Frederick CB, 1993. Personal communication to Munk R. Discussion of results of abstract by Wiegand (1990). Rohm and Haas, Spring House, PA.

Gelbke HP, 1978. Bericht über die Prüfung der akuten Hautreizwirkung von Methylacrylat, Äthylacrylat, Butylacrylat und Äthylhexylacrylat am Kaninchen. BASF, Ludwigshafen.

Ghanayem BI, Maronpot RR and Matthews HB, 1985. Ethyl acrylate-induced gastric toxicity II. Structure-toxicity relationships and mechanism. Tox Appl Pharmacol 80, 336-344.

Gorzinski SJ, Jersey GC, Wade CE, Hermann EA, McCollister SB and Kociba RJ, 1982. Butyl and methyl acrylate: 13-week oral toxicity studies in CDF Fisher 344 rats. Toxicologist 2, 119 [abstract].

Hambly EM and Wilkinson DS, 1978. Contact dermatitis to butyl acrylate in spectacle frames. Contact Dermatitis 4, 115.

Hawley GG, 1981. The Condensed Chemical Dictionary, 10th ed. Van Nostrand Reinhold, New York.

Hijazi N, Chai R, Amster M and Duffee R, 1983. Indoor organic contaminants in energy efficient buildings. In: Frederick ER (ed.) Proc spec conf measurement and monitoring of non-criteria (toxic) contaminants, Chicago, 22-24 March 1983. Air Pollution Control Association, Pittsburgh, PA, 471-477.

Hofmann HT and Klimisch H-J, 1980. Bestimmung der akuten Inhalationstoxiziät $LC_{50}$ von Butylacrylat als dampf bei 4stündiger Exposition an Sprague-Dawley-Ratten. BASF, Ludwigshafen.

ILO (International Labour Office), 1991. Occupational exposure limits for airborne toxic substances, 3rd ed. Occupational Safety and Health Series 37. ILO, Geneva.

INRS (Institut National de Recherches Scientifiques), 1988. Produits chimiques cancérogènes pour l'homme. Cahiers de notes documentaires 132, 489.

Jordan WP, 1975. Cross-sensitization patterns in acrylate allergies. Contact Dermatitis 1, 13-15.

Juhnke I and Lüdemann D, 1978. Ergebnisse der Untersuchung von 200 chemischen Verbindungen auf akute Fischtoxizität mit dem Goldorfentest. Z Wasser-Abwasser-Forschung 11, 161-164.

Kanerva L, Estlander T and Jolanki R, 1988. Sensitization to patch test acrylates. Contact Dermatitis 18, 10-15.

Klimisch H-J, Deckardt K and Mirea D, 1978. Bericht über die Prüfung der subakuten Toxizität von *n*-Butylacrylat. BASF, Ludwigshafen.

Kollár V and Kemka R, 1983. Passive Dosimetrie chemischer Schadstoffe in der Arbeitsluft. Bezpecna Praca 14, 65-68.

Kollár V, Kemka R and Tölgyessy J, 1987. Passive dosimeters and their comparison with the standard method of determination of contaminants in working atmosphere. Chem Papers 41, 235-246.

Kollár V, Kemka R and Tölgyessy J, 1988. Determination of methyl methacrylate, butyl acrylate and n-butyl alcohol in working atmosphere. Chem Papers 42, 161-173 [Chem Abstr 9, 452].

Kopecký J, Linhart I, Stiborová A and Šmejkal J, 1985. Biotransformace esterů akrylové kyseliny u potkana I. Vznik merkapturových kyselin a jejicjh stanovení v moči [Biotransformation of acrylic acid esters in the rat. I. Formation of mercapturic acids and their determination in urine]. Prac Lék 37, 126-129 [Czech; summary].

Kotlovsky Yu V, Grishanova A Yu, Mishin VM and Bachmanova GI, 1988. [Role of rat liver microsomal fractions in the metabolism of methyl methacrylate to formaldehyde]. Vopr Med Khim 34, 14-17. [Russian]

Kuželová M, Kovařík J, Fiedlerová D and Popler A, 1981. Akrylové sloučeniny a zdravotní stav exponovaných osob [Acrylic compounds and general health of the exposed persons]. Pracov Lék 33, 95-99. [Czech; Doc. Occup. Health 8, 1612; Chem. Abstr. 96, 24169v]

Kuželová M, Kovařík J, Fiedlerová D and Popler A, 1981. Akrylové sloučeniny a zdravotní stav exponovaných osob [Acrylic compounds and general health of the exposed persons]. Pracov Lék 33, 95-99. [Czech; Doc. Occup. Health 8, 1612; Chem. Abstr. 96, 24169v]

Legiec IA and Kosson DS, 1988. *In-situ* extraction of industrial sludges. Environ Progress 7, 270-278.

Levine BB, 1960. Studies on the mechanism of the formation of the penicillin antigen I: Delayed allergic cross-reactions among penicillin G and its degradation products. J Exp Med 112, 1131-1157.

Linhart I, Hrabal R, Šmejkal J and Mitera J, 1994. Metabolic pathways of 1-butyl[3-$^{13}$C]acrylate. Indenfication of urinary metabolites in rat using nuclear magnetic resonance and mass spectroscopy. Chem Res Toxicol 7, 2-8.

Lyman WJ, Reehl WF and Rosenblatt DN (eds), 1990. Handbook of chemical property estimation methods. Am Chem Soc, Washington DC, 5.1-30.

Mackay D and Paterson S, 1981. Calculating fugacity. Environ Sci Technol 15, 1006-1014.

Magnusson B and Kligman AM, 1970. Allergic contact dermatitis in the guinea pig. Thomas, Springfield, Illinois.

Maguire HC and Chase MW, 1972. Studies on the sensitization of animals with simple chemical compounds XIII: Sensitization of guinea pigs with picric acid. J Exp Med 132, 357-375.

Marks TA and Jones-Prince C, 1982. Teratological evaluation of *n*-butyl acrylate in CD1 mice. Teratogenic potential of environmental agents, contract contract NO1-ES-6-2127 [raw data and status report to NIEHS]. Prepared by Research Triangle Institute. Rohm and Haas, Spring House, PA.

McCarthy, 1984. Personal communication to D. Ferguson, August 20, 1984 [genotoxicity, reproductive and carcinogenicity testing results for simple acrylates, simple methacrylates, substituted acrylates/methacrylates and multifunctional acrylates/methacrylates]. Rohm and Haas, Philadelphia, PA.

Merkle J and Klimisch H-J, 1983. *n*-Butyl acrylate: Prenatal inhalation toxicity in the rat. Fundam. Appl. Toxicol. 3, 443-447.

Miller RR, Ayres JA, Rampy LW and McKenna MJ, 1981. Metabolism of acrylate esters in rat tissue homogenates. Fund and Applied Tox 1, 410-414.

Murphy SR and Davies JH, 1991. Butyl acrylate. In: Health effects assessments of the basic acrylates. BAMM, Washington, DC.

Nachreiner DJ and Dodd DE, 1989. Butyl acrylate: Acute vapor inhalation toxicity test in rats. Bushy Run Research Center project report 51-575. Union Carbide, Export, PE.

Oberly R and Tansy MF, 1985. $LC_{50}$ values for rats acutely exposed to vapors of acrylic and methacrylic acid esters. J Toxicol Environ Health 16, 811-822.

OECD (Organisation for Economic Co-operation and Development), 1993. Guidelines for the testing of chemicals 2, guideline 209 (adopted 4 April 1984). OECD, Paris.

Oesch F, 1977. Ames-test an den Substanzen Acrylsäure, Methylacrylat, Butylacrylat. Pharmakologisches Institut der Universität Mainz. BASF, Ludwigshafen.

Oettel H and Hofmann HT, 1958. Bericht über die toxikologische Prüfung verschiedener Acrylsäureester. BASF, Ludwigshafen.

Oettel H and Zeller H, 1958. Bericht über die Prüfung der Haut- und Schleimhautreizwirkung verschiedener Acrylsäureester. BASF, Ludwigshafen.

Oettel H and Hofmann HT, 1960a. Bericht über die toxikologische Prüfung verschiedener Acrylsäureester an Kaninchen und Katzen. BASF, Ludwigshafen.

Oettel H and Hofmann HT, 1960b. Subakute Toxizität verschiedener Acrylsäureester. BASF, Ludwigshafen.

Parker D and Türk JL, 1977. Sensitisation with Cr Ni and Zr salts and allergic type granuloma formation in the guinea pig. J Invest Derm 68, 341-345.

Parker, D. and Turk, J.L. (1983). Contact sensitivity to acrylate compounds in guinea pigs. Contact Dermatitis 9, 55-60.

Pellizzari ED, 1977. Analysis of organic air pollutants by gas chromatography and mass spectroscopy. Research Triangle Institute report EPA-600/2-77-100. EPA, Research Triangle Park, NC [NTIS, Springfield, VA].

Peterson LG, 1979. Pers comm of 3 Sep 79 to Zeller H, BASF. Carnegie-Mellon Institute of Research, Pitsburgh PA.

Reinert KH, 1987. Aquatic toxicity of acrylates and methacrylates: quantitative structure-activity relationships based on $K_{ow}$ and $LC_{50}$. Regul Toxicol Pharmacol 7, 384-389.

Reininghaus W, Koestner A and Klimisch H-J, 1991. Chronic toxicity and oncogenicity of inhaled methyl acrylate and *n*-butyl acrylate in Sprague-Dawley rats. Fd Chem Toxic 29, 329-339.

Samimi BS, 1987. The effect of face air velocity on the rate of sampling of air contaminants by a diffusive sampler. In: Berlin A and Brown RH (eds) Diffuse sampling: an alternative approach to workplace air monitoring. Proceedings of an International Symposium, Luxembourg, 22-26 September. Commission of the European Communities, 166-169 (EUR 10555).

Samimi B and Falbo L, 1982. Monitoring of workers exposure to low levels of airborne monomers in a polystyrene production plant. Am Ind Hyg Assoc J 43, 858-862.

Samimi B and Falbo L, 1983. Validation of abcor (NMS) organic vapor dosimeter under various concentrations and air velocity conditions. Am Ind Hyg Assoc J 44, 402-408.

Samimi B and Falbo L, 1985. Comparison of standard charcoal tubes with abcor (NMS) gasbadges within controlled atmosphere. Am Ind Hyg Assoc G 46, 49-52.

Sanders JM, Burka LT and Matthews HB, 1988. Metabolism and disposition of *n*-butyl acrylate in male Fischer rats. Drug Metabolism and Disposition 16, 429-434.

Sapota A, 1991. The dynamics of distribution and excretion of butyl-(2,3-$^{14}$C)-acrylate in male Wistar albino rats. Polish J Occup Med Environ Health 4, 55-66.

Sapota A and Jakubowski M, 1990. Distribution des 2,3-$^{14}$C-acrylates de méthyle, de butyle et de 2-éthylhexyle chez rat mâle albinos Wistar. Cah Notes Doc 40, 678-682.

Schafer EW, Bowles WA and Hurlbut J, 1983. The acute oral toxicity, repellency and hazard potential of 998 chemicals to one or more species of wild and domestic birds. Arch Environ Contam Toxicol 12, 355-382.

Smyth HF, Carpenter CP and Weil CS, 1951. Range-finding toxicity data, list IV. AMA Archiv Industr Hyg Occup Med 4, 119-122.

Sokal J, Barański B, Czajkowska T, Krysiak B, Majka J, Szendzikowski S, Stetkiewicz J and Tarkowski S, 1980. Preliminary project of the standard minimal scope and methods of testing acute toxicity of industrial chemical substances. Pol J Pharmacol Pharm 32, 223-229.

SRI International, 1987. Acrylic acids and acrylic esters. In: SRI International. International directory of chemical producers in Western Europe. SRI International, Menlo Park, CA.

SRI International, 1990. Acrylic acid and esters. Chemical Economics Handbook. SRI International, Menlo Park, CA.

Stott WT and McKenna MJ, 1985. Hydrolysis of several glycol ether acetates and acrylate esters by nasal mucosal carboxylesterase *in vitro*. Fund Appl Tox 5, 399-404.

Svetlakov AV, Ivanov VV, Fefelova A, Golounin AV, 1989. [Body distribution and interaction of rat blood proteins with butyl acrylic and methacrylic acid]. Gi Tr Prof Zab 3, 51-52 [Russian].

Tanii H and Hashimoto K, 1982. Structure-toxicity relationship of acrylates and methacrylates. Toxicol. Letters 11, 125-129.

Tschernikowa WW, Astapowa SA, Gisatullina NS, Efremenko AA, Kustowa ZR, Lobanowa IJa, Ostroumowa NA, Sawtschenko NA, Stepanow SW and Tiunowa LW, 1979. [Experimental studies of acute and chronic effect of butylacrylate]. Khim Prom st, Ser, Toksikol Sanit Khim Plastmass 2, 22-24.

UK-HSE (Health and Safety Executive), 1992. Bytyl acrylate. In: Occupational exposure limits 1992. HMSO, London.

US-NTP (US National Toxicology Programme), 1991. *In vitro* cytogenetics data on *n*-butyl acrylate. Unpublished results. NTP Research Triangle Park, NC.

Van der Walle HB, Delbressine LPC and Seutter E, 1982a. Concomitant sensitization to hydroquinone and *p*-methoxyphenol in the guinea pig, inhibitors in acrylic monomers. Contact Dermatitis 8, 147-154.

Van der Walle HB, Klecak G, Geleick H and Bensink T, 1982b. Sensitizing potential of 14 mono(meth)acrylates in the guinea pig. Contact Dermatitis 8, 223-235.

Vernot EH, MacEwen JD, Haun CC and Kinkead ER, 1977. Acute toxicity and skin corrosion data for some organic and inorganic compounds and aqueous solutions. Toxicol Appl Pharmacol 42, 417-423.

Vodička P, Gut I and Frantik E, 1990. Effects of inhaled acrylic acid derivatives in rats. Toxicology 65, 209-221.

Waegemaekers THJM and Bensink MPM, 1984. Non-mutagenicity of 27 aliphatic acrylate esters in the *Salmonella*-microsome test. Mutation Res 137, 95-102.

Weiss G, 1986. *n*-Butyl acrylate. Hazardous chemicals databook, 2nd ed. Noyes Data, Park Ridge, NJ, 192.

Wiegand H, 1990. Species differences in the metabolism of *n*-butyl acrylate. Presented at: 31st spring meeting, Deutsche Gesellschaft für Pharmakologie und Toxikologie, Mainz [abstract].

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

Yocom JE, Hijazi NH and Zoldak JJ, 1984. Use of direct analysis mass spectrometry to solve indoor air quality problems. Proc Internat Conf Indoor Air Quality, Clin, 3rd ed, 245-250.

Zeller H and Klimisch H-J, 1979. Bericht über die Bestimmung der akuten Inhalations- toxizitaet $LC_{50}$ von Butylacrylat bei 4stündiger Exposition an Sprague-Dawyley-Ratten (nüchtern), Sprague-Dawley-Ratten (gefüttert), NMRI-Maeusen (nüchtern), NMRI-Mäusen (gefüttert), Chin Streifenhamster (nüchtern), Chin Streifenhamster (gefüttert). BASF, Ludwigshafen.

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