BUTYL ACRYLATE
(CAS Reg. No. 141-32-2)

INTERIM ACUTE EXPOSURE GUIDELINE LEVELS
(AEGLs)

For
NAS/COT Subcommittee for AEGLs

Oak Ridge National Laboratory, managed by UT-Battelle, LLC., for the U.S. Dept. of Energy under contract DE-AC05-00OR22725
PREFACE

Under the authority of the Federal Advisory Committee Act (FACA) P. L. 92-463 of 1972, the National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances (NAC/AEGL Committee) has been established to identify, review and interpret relevant toxicologic and other scientific data and develop AEGLs for high priority, acutely toxic chemicals.

AEGLs represent threshold exposure limits for the general public and are applicable to emergency exposure periods ranging from 10 minutes to 8 hours. Three levels — AEGL-1, AEGL-2 and AEGL-3 — are developed for each of five exposure periods (10 and 30 minutes, 1 hour, 4 hours, and 8 hours) and are distinguished by varying degrees of severity of toxic effects. The three AEGLs are defined as follows:

AEGL-1 is the airborne concentration (expressed as parts per million or milligrams per cubic meter [ppm or mg/m³]) of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic, non-sensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure.

AEGL-2 is the airborne concentration (expressed as ppm or mg/m³) of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape.

AEGL-3 is the airborne concentration (expressed as ppm or mg/m³) of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening health effects or death.

Airborne concentrations below the AEGL-1 represent exposure levels that could produce mild and progressively increasing but transient and nondisabling odor, taste, and sensory irritation or certain asymptomatic, non-sensory effects. With increasing airborne concentrations above each AEGL, there is a progressive increase in the likelihood of occurrence and the severity of effects described for each corresponding AEGL. Although the AEGL values represent threshold levels for the general public, including susceptible subpopulations, such as infants, children, the elderly, persons with asthma, and those with other illnesses, it is recognized that individuals, subject to unique or idiosyncratic responses, could experience the effects described at concentrations below the corresponding AEGL.
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SUMMARY

n-Butyl acrylate (BA) is a flammable liquid that is slightly soluble in water and miscible with most organic solvents (ECETOC 1994). BA is an acrylate monomer used to prepare homopolymers and copolymers with other monomers. The chemical reacts readily with numerous organic and inorganic compounds so it is used as a starting product for chemical synthesis (ECETOC 1994). BA is also used in surface coatings, leather finishes, adhesives, paper coatings, fibers, plastics, and resins (Bisesi 2001; ECETOC 1994). BA is the largest-volume production commodity acrylate ester (Lacson et al. 2001).

Few data were available concerning human exposures to BA and none of the data were suitable for derivation of any AEGL values. Worker monitoring studies reported up to 10.5 ppm as a short-term exposure average concentration (Rohm and Haas, Co. 1987), but no health effects were included.

Few animal data were available for derivation of AEGL-1 values. In a developmental toxicity study (Rohm and Haas Co. 1992; Merkle and Klimisch 1983), no clinical signs were reported for rats exposed repeatedly to 25 ppm. Clinical signs reported in other studies were too severe for AEGL-1 (concentrations of 135 ppm and higher resulted in eye and nasal discharge, dyspnea, gasping). The no-effect level for respiratory depression in mice was 30 ppm (Kirkpatrick 2003). A concentration of 25 ppm was chosen as a concentration below AEGL-1 effects. Extrapolations were not performed. A total uncertainty factor of 3 was used including a 1 for interspecies extrapolation and 3 for intraspecies extrapolation. Use of greater uncertainty factors was not necessary because the mechanism of irritation is not expected to differ between individuals.

The best animal data relevant to derivation of AEGL-2 are from a subchronic study in which male and female Sprague-Dawley rats (n = 20) were exposed to 0, 21, 108, 211, or 546 ppm BA for 6 hours/day, 5 days/week, for 13 weeks (Klimisch et al. 1978). At the highest concentration, mortality, reduced body weight gain, and clinical signs of bloody ocular and nasal discharges and rhinitis were observed; marked lesions of the respiratory tract were found at necropsy. At 211 ppm all animals survived but had reduced body weight gain and showed bloody ocular and nasal discharges; slight edema and erosion of the nasal mucosa were observed histologically in a few individuals. Slight decreases in weight gain but no histopathological changes were observed in animals exposed to 108 ppm. The NOAEL was 21 ppm. In other studies, no maternal or developmental toxicity was seen in rats repeatedly exposed to 25 or 100 ppm during gestation (Rohm and Haas Co. 1992; Merkle and Klimisch 1983; Saillenfait et al. 1999).

The concentration of 211 ppm for 6 hours/day was used as the basis for AEGL-2 derivation. Values were scaled using the equation C^n × t = k where n ranges from 0.8 to 3.5 (ten Berge et al. 1986). In the absence of an empirically derived, chemical-specific exponent, scaling was performed using n = 3 for extrapolating to the 30-minute and 1- and 4-hour time points and n = 1 for the 8-hour time point. A total uncertainty factor of 3 was used including 1 for interspecies extrapolation and 3 for intraspecies extrapolation. Use of greater uncertainty factors was not necessary because the mechanism of irritation is not expected to differ between individuals.

According to Section 2.7 of the Standing Operating Procedures for Developing Acute Exposure
Guideline Levels for Hazardous Chemicals (NRC 2001), 10-minute values are not to be scaled from an experimental exposure time of ≥4 hours. Therefore, the 30-minute AEGL-2 value was also adopted as the 10-minute value.

The best animal data relevant to derivation of AEGL-3 values is the Oberly and Tansy (1985) 4-hour LC$_{50}$ study in rats. This was a well conducted study with a wide range of analytically determined exposure concentrations. Clinical signs of irritation were observed in animals during exposure and death was attributed to cardiopulmonary collapse. The calculated 4-hour LC$_{50}$ value was 2730 ppm. From these data a 4-hour BMCL$_{05}$ value was calculated by a log-probit analysis using US EPA Benchmark Dose Software version 1.3.2. The resulting 4-hour BMCL$_{05}$ of 1652 ppm was used to derive the 30-minute, and 1-, 4- and 8-hour AEGL-3 values. Values were scaled using the equation $C^n \times t = k$ where $n$ ranges from 0.8 to 3.5 (ten Berge et al. 1986). A value of $n = 1.3$ was calculated by combining 1- and 4-hour LC$_{50}$ data sets from ethyl acrylate (NAC 2004) in a 3-dimensional probit analysis (Zwart et al. 1992). Use of an $n$ value calculated from a structurally related chemical was considered appropriate because the mechanism leading to death is similar for both compounds. A total uncertainty factor of 10 was used including 3 for interspecies extrapolation and 3 for intraspecies extrapolation. Use of greater uncertainty factors was not necessary because the mechanism of toxicity (local damage in the lower airways/lungs) is not expected to differ between individuals. According to Section 2.7 of the Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals (NRC 2001), 10-minute values are not to be scaled from an experimental exposure time of ≥4 hours. Therefore, the 30-minute AEGL-3 value was also adopted as the 10-minute value.

The reported odor threshold concentrations are not sufficiently qualified to derive a level of odor awareness (LOA) according to van Doorn et al. (2002).

The calculated values are listed in the tables below.

### Summary of AEGL Values for Butyl Acrylate

<table>
<thead>
<tr>
<th>Classification</th>
<th>10-minute</th>
<th>30-minute</th>
<th>1-hour</th>
<th>4-hour</th>
<th>8-hour</th>
<th>Endpoint (Reference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEGL–1 (Nondisabling)</td>
<td>8.3 ppm (44 mg/m$^3$)</td>
<td>8.3 ppm (44 mg/m$^3$)</td>
<td>8.3 ppm (44 mg/m$^3$)</td>
<td>8.3 ppm (44 mg/m$^3$)</td>
<td>8.3 ppm (44 mg/m$^3$)</td>
<td>No clinical signs with repeated exposures (Rohm and Haas Co. 1992; Merkle and Klimisch 1983)</td>
</tr>
<tr>
<td>AEGL–2 (Disabling)</td>
<td>160 ppm (850 mg/m$^3$)</td>
<td>160 ppm (850 mg/m$^3$)</td>
<td>130 ppm (690 mg/m$^3$)</td>
<td>81 ppm (430 mg/m$^3$)</td>
<td>53 ppm (280 mg/m$^3$)</td>
<td>Clinical signs and histopathology with repeated exposure (Klimisch et al. 1978)</td>
</tr>
<tr>
<td>AEGL–3 (Lethal)</td>
<td>820 ppm (4400 mg/m$^3$)</td>
<td>820 ppm (4400 mg/m$^3$)</td>
<td>480 ppm (2600 mg/m$^3$)</td>
<td>170 ppm (906 mg/m$^3$)</td>
<td>97 ppm (520 mg/m$^3$)</td>
<td>Calculated BMCL$<em>{05}$ from LC$</em>{50}$ data (Oberly and Tansy 1985)</td>
</tr>
</tbody>
</table>

**References**

n-BUTYL ACRYLATE

Interim 1: 08/2007


<http://ceh.sric.sri.com/Public/Reports/606.4000/>


1. INTRODUCTION

n-Butyl acrylate (BA) is a flammable liquid that is slightly soluble in water and miscible with most organic solvents (ECETOC 1994). BA is an acrylate monomer used to prepare homopolymers and copolymers with other monomers. The chemical reacts readily with numerous organic and inorganic compounds so it is used as a starting product for chemical synthesis (ECETOC 1994). BA is also used in surface coatings, leather finishes, adhesives, paper coatings, fibers, plastics, and resins (Bisesi 2001; ECETOC 1994).

BA is the largest-volume production commodity acrylate ester (Lacson et al. 2001). In 1993, the United States produced 340 million kg BA (HSDB 2004) which increased to >454 million kg in 2002 (U.S. EPA 2004). The most common manufacturing process is by catalyzed esterification of acrylic acid with n-butanol (ECETOC 1994).

Selected chemical and physical properties of BA are listed in Table 1.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synonyms</td>
<td>2-propenoic acid butyl ester</td>
<td>O’Neil et al. 2001</td>
</tr>
<tr>
<td>Chemical formula</td>
<td>C₇H₁₂O₂</td>
<td>O’Neil et al. 2001</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>128.17</td>
<td>O’Neil et al. 2001</td>
</tr>
<tr>
<td>CAS Reg. No.</td>
<td>141-32-5</td>
<td></td>
</tr>
<tr>
<td>Physical state</td>
<td>liquid</td>
<td>O’Neil et al. 2001</td>
</tr>
<tr>
<td>Solubility in water</td>
<td>0.14 g/100 mL at 20°C</td>
<td>O’Neil et al. 2001</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>4.3 mmHg at 20°C</td>
<td>ECETOC 1994</td>
</tr>
<tr>
<td>Vapor density (air =1)</td>
<td>4.4</td>
<td>ECETOC 1994</td>
</tr>
<tr>
<td>Liquid density (water =1)</td>
<td>0.8986</td>
<td>O’Neil et al. 2001</td>
</tr>
<tr>
<td>Melting point</td>
<td>-64°C, approximately</td>
<td>ECETOC 1994</td>
</tr>
<tr>
<td>Boiling point</td>
<td>145°C</td>
<td>O’Neil et al. 2001</td>
</tr>
<tr>
<td>Auto-ignition</td>
<td>267°C</td>
<td>ECETOC 1994</td>
</tr>
<tr>
<td>Conversion factors</td>
<td>1 ppm = 5.33 mg/m³</td>
<td>ECETOC 1994</td>
</tr>
<tr>
<td></td>
<td>1 mg/m³ = 0.188 ppm</td>
<td></td>
</tr>
</tbody>
</table>

2. HUMAN TOXICITY DATA

2.1. Acute Lethality

No reports of human fatalities from exposure to BA were found.
2.2. Nonlethal Toxicity

2.2.1. Odor Threshold/Odor Awareness

AIHA (1995a) listed the range of reported odor thresholds as 0.00096-0.10 ppm; however, all values were from either unpublished data or anonymous references.

2.2.2. Case Reports

Contact dermatitis to BA has been demonstrated with patch testing (Hambly and Wilkinson 1978), but no reports of respiratory sensitization were found.

2.2.3. Epidemiologic Studies/Occupational Exposures

No epidemiologic studies were found concerning human exposures to BA.

Tuček et al. (2002) conducted a prospective cohort study during 1992-1999 of workers involved in the production of acrylic acid and its esters. Groups of 60 controls and 60 exposed individuals were followed with the average exposure period for the exposed group 13±5 years. Exposures to up to eight chemicals, including BA, were determined by personal passive dosimetry. Concentrations of all chemicals remained low, however, the maximum allowable concentration for BA (not specified) was exceeded for 2% of the measurements. Throughout the study chemical workers did not show any health-related changes as measured by interview, general medical examination, hematology, clinical chemistry, serum immunity parameters, selected tumor markers, and spirometry. Subjective complaints at the workplace of burning eyes and throat, occasional irritating cough, headaches, and less frequently nausea or dizziness, and fleeting dermatological complaints were reported by approximately 40% of the exposed workers; the study authors did not correlate symptoms with exposure concentrations. In contrast only 20% of the controls reported subjective complaints with symptoms associated with ergonomics.

Rohm and Haas, Co. (1987) submitted employee exposure monitoring results for a number of operations during 1978-1987. Average concentrations of BA for full shift ranged from 0.1-1.0 ppm and short-term exposure average concentrations ranged from 0.4-10.5 ppm. No other information was included in the report.

Time-weighted average concentrations of BA at four job sites in a polystyrene production plant were 12-93 ppb (range: not detected-270 ppb) in the breathing zone of workers and 1-93 ppb (range: not detected-525 ppb) in the atmosphere of the workplaces (Samimi and Falbo 1982). Samples were collected in charcoal tubes from 50 minutes to 7.5 hours and quantitated with a gas chromatograph. No information on worker health status was given.

2.2.4. Clinical Studies

Olfactory function was investigated in chemical workers exposed to acrylates and methacrylates (Schwartz et al. 1989; Rohm and Haas 1988). Specific chemicals were not identified. Workers were administered a standardized smell identification test consisting of an
odorant strip and a questionnaire. A dose-responsive relationship was found between olfactory
dysfunction and cumulative exposure scores (semi-quantitative indices of life-time exposures to
the acrylates) with reversible effects shown with increasing duration since the last exposure.

A number of studies have shown positive results for skin sensitization with patch testing. In
a summary of these studies (BIBRA 1991), it was emphasized that it was impossible to conclude
whether the reactions were to primary sensitization to BA or to cross-reactivity to other
acrylates.

2.3. Neurotoxicity

No reports of neurotoxicity in human from exposure to BA were found.

2.4. Developmental/Reproductive Toxicity

No information was found regarding the reproductive or developmental toxicity of BA in
humans.

2.5. Genotoxicity

No information was found regarding the genotoxic effects of BA in humans.

2.6. Carcinogenicity

No information was found regarding the carcinogenicity of BA in humans. IARC (1999)
lists BA as not classifiable as to its carcinogenicity to humans due to lack of data in humans and
inadequate evidence in experimental animals.

2.7. Summary

Very little information is available concerning human exposure to BA. Symptoms of
irritation were occasionally reported in chemical plant workers. Dermal sensitization has been
reported but not respiratory sensitization.

3. ANIMAL TOXICITY DATA

3.1. Acute Lethality

3.1.1. Hamsters

Groups of 10 male and 10 female Chinese hamsters were exposed to a mean analytical
concentration of 817 ppm BA for 6 hours/day for 4 days (Engelhardt and Klimisch 1983). Four
males died during the exposure period. Clinical signs of toxicity were listed as dyspnea,
disequilibrium, and bloody discharge from the eyes and noses; no further details were given.
BASF (1979a) reported 4-hour LC$_{50}$ values for male and female Chinese hamsters (n = 10/sex/group) of 1201-1654 ppm. No further study details were given.

3.1.2. Rats

Male Sprague-Dawley rats (n = 10/group) were exposed whole body for 4 hours to 1990, 2035, 2500, 2828, or 3041 ppm BA followed by a 14-day observation period (Oberly and Tansy 1985). Atmospheres were generated by constant infusion of liquid monomer into a heated reaction vessel through which room air was passed at a known constant rate. Vapor concentration was determined by gas chromatography. During exposures animals had normal behavior during the first few minutes then exhibited irritation of the eyes, nose, and respiratory tract and labored breathing. All deaths occurred within 24 hours and were attributed to cardiopulmonary collapse. The number of deaths at each concentration was 0, 1, 3, 5, and 7, respectively. The 4-hour LC$_{50}$ was calculated as 2730 ppm.

BASF (1979b,c, 1980) reported 4-hour LC$_{50}$ values for male and female Sprague-Dawley rats (n = 10/sex/group) of 2140-2415 and 2405-2685 ppm, respectively, following whole body exposure and 2140 and 1910 ppm, respectively, following nose-only exposure. Atmospheres were generated by using a permanent infusion pump to add a constant concentration of the testing substance to a heated vaporizer; the vapor was then mixed with fresh air. The analytical method was not described. Clinical signs indicative of severe irritation were observed in animals at concentrations of 677 ppm and above and deaths occurred at concentrations of 1278 ppm and above.

Two older sources list lethality in rats exposed to 1000 ppm BA for 4 hours as 5/6 (Smyth et al. 1951) and 1/6 (Carpenter et al. 1974). No further information was available in either reference.

3.1.3. Mice

BASF (1979d,e) reported 4-hour LC$_{50}$ values for male and female NMRI mice (n = 10/sex/group) of 1290 and 1285 ppm, respectively, for fed animals and 1315 and 1415 ppm, respectively, for fasted animals. Animals were exposed whole body in dynamic chambers. Atmospheres were generated by using a permanent infusion pump to add a constant concentration of the testing substance to a heated vaporizer; the vapor was then mixed with fresh air. The analytical method was not described. Clinical signs indicative of irritation included lacrimation, nasal discharge, and dyspnea.

3.2. Nonlethal Toxicity

3.2.1. Rats

Groups of 10 male and 10 female Sprague-Dawley rats were exposed by whole body to a mean analytically determined concentration of 820 ppm BA for 6 hours/day for 4 days (Engelhardt and Klimisch 1983). No deaths were reported. Clinical signs of toxicity were listed
as dyspnea, disequilibrium, and bloody discharge from the eyes and noses; no further details were given.

3.2.2. Mice

Groups of male Swiss Webster mice (n = 8/group) were exposed head-only to 30-900 ppm BA for 30 minutes (Kirkpatrick 2003). Test atmospheres were generated by mixing chemical vapor with fresh air using a calibrated rotameter-type flowmeter. Concentrations were measured by gas chromatography. No treatment-related deaths occurred during exposure to any concentration and clinical signs were not reported. The calculated RD₅₀ was 340 ppm. The lowest effect level for respiratory depression was 100 ppm (-9%) and the no effect level was 30 ppm.

3.3. Neurotoxicity

No information was found on the neurotoxicity of BA in animals following inhalation exposure.

3.4. Developmental/Reproductive Toxicity

Groups of 30 female Sprague-Dawley rats were administered BA at concentrations of 0, 25, 135, or 250 ppm for 6 hrs/day, on gestation days 6-15 (Rohm and Haas Co. 1992, Merkle and Klimisch 1983). Mean analytically determined concentrations during the study were 25, 137, and 251 ppm, respectively. All dams survived to scheduled sacrifice on GD 20. During exposure to 135 ppm, animals had pronounced eye and nasal discharge and ruffled fur; these signs were more pronounced during exposure to 250 ppm and also included closed eyes and matted fur. Concentration-related decreases in maternal body weight gain were observed during the exposure interval at the two highest concentrations. Maternal necropsy revealed loss of fatty tissue in two mid- and nine high-concentration animals. No differences between the treated and control groups were found for numbers of corpora lutea and implantations or fetal and placental weights. Concentration-related decreases in live fetuses and subsequent increases in resorptions occurred at the two highest concentrations. In the control, low-, mid-, and high-concentration groups, the mean number of live fetuses/dam was 11.5, 10.6, 8.8, and 8.4, respectively, and the mean percent resorptions per dam was 11.6, 13.8, 23.6, and 31.0, respectively. No treatment-related external, visceral, or skeletal malformations were observed in any fetus.

In another study, Sprague-Dawley rats (n = 24-25) were administered 0, 100, 200, or 300 ppm BA, 6 hr/day on GD 6-20 (Saillenfait et al. 1999). Mean analytically determined concentrations were 103.3, 202.8, and 302.5 ppm, respectively. All animals survived to scheduled sacrifice; clinical signs of toxicity were not reported. Maternal body weight gain was markedly reduced in the mid- and high-concentration groups during the exposure interval to 56% and 13%, respectively, of the control group level. Food consumption was also decreased for these treated groups. In contrast to the study described above, the numbers of implantation sites, live fetuses, and resorptions per litter were not affected. Fetal body weights were significantly reduced in the 200 and 300 ppm groups. No treatment-related external, visceral, or skeletal malformations were found in any fetus.
3.5. Genotoxicity

BA, at concentrations up to 2000 µg/plate, was not mutagenic in *Salmonella typhimurium* (TA1535, TA1537, TA1538, TA98, TA100) with and without metabolic activation (Waegemaekers and Bensink 1984). With Syrian hamster embryo cells, the chemical was negative in *in vitro* tests for micronucleus formation (Wiegand et al. 1989; Fritzenschaf et al. 1993) and unscheduled DNA synthesis (Wiegand et al. 1989).

Male and female Sprague-Dawley rats and Chinese hamsters were exposed to mean concentrations of 820 ppm or 817 ppm, respectively, for 6 hours/day for 4 days. Cytogenetic analysis of bone marrow did not show any indication of increased chromosomal aberrations (Engelhardt and Klimisch 1983).

3.6. Subchronic and Chronic Toxicity/Carcinogenicity

Male and female Sprague-Dawley rats (*n* = 20) were exposed to 0, 21, 108, 211, or 546 ppm BA for 6 hours/day, 5 days/week, for 13 weeks (Klimisch et al. 1978). At the highest concentration, 31/40 animals died during weeks 3-13 following reduced body weight gain and clinical signs of bloody ocular and nasal discharges and rhinitis. Necropsy of these animals revealed hyperemic nasal mucosa, edematous nasal epithelium, metaplasia of the olfactory epithelium, extensive and advanced necrosis of the lungs associated with bacteria, cornification of the epithelium of the trachea and bronchi, pulmonary hyperemia, and pneumonia. At 211 ppm all animals survived but had reduced body weight gain and showed bloody ocular and nasal discharges; slight edema and erosion of the nasal mucosa were observed histologically in a few individuals. Slight decreases in weight gain but no histopathological changes were observed in animals exposed to 108 ppm. The NOAEL was 21 ppm.

In a 2-year inhalation study followed by a 6-month recovery, male and female Sprague-Dawley rats (*n* = 86) were exposed to 0, 15, 45, or 135 ppm BA for 6 hours/day, 5 days/week; the concentrations were 0, 5, 15, and 45 ppm for the first 13 weeks (Reininghaus et al. 1991). No clinical signs or systemic toxicity were observed and no evidence of carcinogenicity was found. Histopathological lesions attributable to chronic irritation were seen in the nasal mucosa (concentration-related increases in all groups) and cornea (135-ppm groups).

3.7. Summary

BA caused clinical signs of irritation in all species tested. LC₅₀ values were not substantially different between hamsters, rats, and mice; however in one study (Engelhardt and Klimisch 1983) hamsters appeared to be more sensitive than rats to the lethal effects of BA. Animal toxicity data are summarized in Table 2.

Embryolethality was found in one developmental toxicity study but not in another study; the reason for the difference in these results is unknown.
### TABLE 2. Summary of toxicity data in laboratory animals exposed to BA

<table>
<thead>
<tr>
<th>Species, duration</th>
<th>LC$_{50}$</th>
<th>Lethal conc.</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hamster (10/sex), 4 h</td>
<td>1201-1654 ppm</td>
<td></td>
<td>BASF 1979a</td>
</tr>
<tr>
<td>Hamster (10/sex), 6 h/day, 4 days</td>
<td>817 ppm; 4/10 males</td>
<td>Engelhardt and Klimisch 1983</td>
<td></td>
</tr>
<tr>
<td>Rat (10 m), 4 h</td>
<td>2730 ppm</td>
<td></td>
<td>Oberly and Tansy 1985</td>
</tr>
<tr>
<td>Rat (10/sex), 4 h</td>
<td>1936-2500 ppm</td>
<td></td>
<td>BASF 1979b,c, 1980</td>
</tr>
<tr>
<td>Rat (10/sex), 6 h/day, 4 days</td>
<td>820 ppm; 0/20</td>
<td>Engelhardt and Klimisch 1983</td>
<td></td>
</tr>
<tr>
<td>Mouse (10/sex), 4 h</td>
<td>1278-1354 ppm</td>
<td></td>
<td>BASF 1979d,e</td>
</tr>
</tbody>
</table>

## 4. SPECIAL CONSIDERATIONS

### 4.1. Metabolism and Disposition

Male Fischer 344 rats were administered 4, 40, or 400 mg/kg of [2,3-$^{14}$C]-radiolabeled BA by gavage or 40 mg/kg by intravenous injection (Sanders et al. 1988). The results of this study showed that BA was rapidly absorbed from the gastrointestinal tract and completely metabolized following either route of administration. Gastrointestinal absorption and metabolism were similar over the range of doses used. BA-derived radioactivity was found in all major tissues sampled (blood, liver, kidney, skin, adipose, muscle) with peak concentrations within 15 minutes followed by rapid decline over the next 2 hours; elimination from the tissues was negligible between 2 hours and 3 days. Of the fraction measured in blood, 70% was associated with the red blood cells. BA was completely metabolized and no parent compound was detected in urine, bile, or tissues. BA was mainly hydrolyzed by carboxylesterases to acrylic acid and butanol, with a small portion being directly conjugated with glutathione. The acrylic acid moiety entered intermediary metabolism with 65-78% of the oral dose subsequently excreted as CO$_2$. Small amounts of the mercapturic acids $\text{N}$-acetyl-$\text{S}$-(2-carboxyethyl)cysteine-$\text{S}$-oxide and $\text{N}$-acetyl-$\text{S}$-(2-carboxyethyl)cysteine were detected in urine. Comparisons by route of administration showed a slightly greater portion distributed to adipose tissue, less CO$_2$ excretion, and greater amounts of urinary metabolites following intravenous injection versus oral dosing (Sanders et al. 1988).

A similar metabolic profile was found in female Wistar rats administered 1 mmol/kg of [3-$^{13}$C]-labeled BA by intraperitoneal injection (Linhart et al. 1994a). The major urinary metabolites were 3-hydroxypropanoic acid and the mercapturic acids noted above. Metabolites indicative of metabolic activation of BA were not found. In other work by these authors (Linhart...
et al. 1994b), quantitation of the mercapturic acids showed that the absolute amount remained relatively constant while the proportion conjugated decreased with increasing dose (3.6% at 0.5 mmol/kg to 1.6% at 3 mmol/kg). In addition, characterization of the carboxylic acids found in urine indicated that the acrylic acid entered intermediary metabolism via propanoic acid catabolism and the tricarboxylic acid cycle (Linhart et al. 1994a,b).

Following a 6-hour inhalation exposure of male Wistar rats to 188-752 ppm BA, <3% of the dose was excreted in the urine as thioethers (Vodička et al. 1990). However total tissue sulfhydryl groups were significantly decreased in the liver following exposure to 752 ppm. Non-protein sulfhydryl groups were also decreased in liver and to a lesser extent in blood, brain, and lung.

The activity of carboxylesterase recovered from nasal mucosal tissue of B6C3F1/CrlBr mice was studied with BA (Stott and McKenna 1985). Under subsaturating concentrations, BA was hydrolyzed under first-order kinetics with a $V_{\text{MAX}}$ of $0.141 \times 10^{-3}$ M/min and a $K_m$ of $1.41 \times 10^{-3}$ M. Loss of enzymatic activity occurred at concentrations in excess of 5 mM. Carboxylesterase specific activity was approximately equivalent in the nasal mucosa and liver of mice with ethylene glycol monomethyl ether acetate as substrate. In vitro nasal enzyme activity was shown to be similar between mice and dogs, slightly less in rats, and nearly sevenfold less in rabbits.

Another in vitro study measured the hydrolysis rate in rat liver homogenate and disappearance from whole blood (Miller et al. 1981). The rate of hydrolysis of BA (23.6 nmole•min⁻¹) in liver homogenate directly correlated with the appearance of acrylic acid (26 nmole•min⁻¹) in the medium. In contrast the rate of hydrolysis in whole blood (9.4 nmoles•min⁻¹) was much greater than the production of acrylic acid (4.6 nmoles•min⁻¹) suggesting a different mechanism. This is supported by results with ethyl acrylate in which the ester was shown to bind with non-protein sulfhydryls in red blood cells.

### 4.2. Mechanism of Toxicity

Stott and McKenna (1985) concluded from in vitro experiments that hydrolysis of BA by carboxylesterase activity in nasal mucosa produces acid metabolites which result in the nasal lesions. Subsequently, little BA is available for systemic absorption.

### 4.3. Structure Activity Relationships

The low molecular weight acrylic acid ester monomers are lacrimators and irritants to the eyes, skin, and mucus membranes (Bisesi 2001, Autian 1975). Acute toxicity based on LC₅₀ values for a number of chemicals was determined to be methyl acrylate (1350 ppm) > ethyl acrylate (2180 ppm) > butyl acrylate (2730 ppm) > butyl methacrylate (4910 ppm) > methyl methacrylate (7093 ppm) > ethyl methacrylate (8300 ppm) (Oberly and Tansy 1985). For all the acrylate esters tested by Oberly and Tansy (1985), rats showed signs of irritation of the eyes, nose, and respiratory tract. The rapid metabolism and elimination of the low molecular weight esters suggests that cumulative effects will not occur (Autian 1975).
The target within the respiratory tract was shown to be the olfactory epithelium lining the dorsal meatus following exposure to several acrylate esters. Similar nasal lesions were observed in laboratory animals after exposure to ethyl acrylate (NAC 2004a), methacrylic acid (NAC 2004b), methyl methacrylate (NAC 2004c), and acrylic acid (NAC 2004d).

4.4. Other Relevant Information

4.4.1. Species Variability

Little evidence for species variation was seen in the available data. Clinical signs were similar between hamsters, rats, and mice following exposure to BA.

4.4.2. Susceptible Populations

Little data were available that identified susceptible populations. Developmental toxicity studies show that the fetus is affected at maternally toxic concentrations.

4.4.3. Concentration-Exposure Duration Relationship

The concentration-exposure duration relationship for an irritant gas such as BA can be described by the equation $C^n \times t = k$, where the exponent $n$ ranges from 0.8 to 3.5 (ten Berge et al. 1986). In the absence of a chemical-specific, empirically derived exponent, a default value of $n = 1$ can be used when extrapolating to longer timepoints and a default value of $n = 3$ can be used when extrapolating to shorter timepoints. This method will yield the most conservative AEGL estimates and was used for extrapolation of AEGL-2 values.

Different $n$ values were used in the extrapolation of AEGL-2 and -3. This approach was considered to be appropriate because the mechanism of toxicity for AEGL-2 endpoints differs from that of AEGL-3 endpoints. Under the definition of AEGL-2, lesions in the upper respiratory tract were caused by irritation of the chemical due to direct contact with mucus membranes in conjunction with enzymatic hydrolysis. In contrast, lethality as the basis for AEGL-3 was due to cardiopulmonary collapse as a result of the chemical reaching the lower respiratory tract and the systemic circulation. A value of $n = 1.3$ was calculated by combining 1- and 4- hour $LC_{50}$ data sets from ethyl acrylate (NAC 2004a) in a 3-dimensional probit analysis (Zwart et al. 1992). Use of an $n$ value calculated from a structurally related chemical was considered appropriate because the mechanism leading to death is similar for both compounds.

5. DATA ANALYSIS FOR AEGL-1

5.1. Summary of Human Data Relevant to AEGL-1

No human data relevant to derivation of AEGL-1 values were found. Worker monitoring studies reported up to 10.5 ppm as a short-term exposure average concentration (Rohm and Haas, Co. 1987), but no health effects were included.
5.2. Summary of Animal Data Relevant to AEGL-1

Few animal data were available for derivation of AEGL-1 values. In a developmental toxicity study (Rohm and Haas Co. 1992; Merkle and Klimisch 1983), no clinical signs were reported for rats exposed repeatedly to 25 ppm. Clinical signs reported in other studies were too severe for AEGL-1 (concentrations of 135 ppm and higher resulted in eye and nasal discharge, dyspnea, gasping). The no-effect level for respiratory depression in mice was 30 ppm (Kirkpatrick 2003).

5.3. Derivation of AEGL-1

Limited data were available upon which to base AEGL-1 values. A concentration of 25 ppm, which did not result in any effects in pregnant rats following repeated exposures, was chosen as a concentration below the threshold for AEGL-1 effects. Extrapolations were not performed. A total uncertainty factor of 3 was used including 1 for interspecies extrapolation and 3 for intraspecies extrapolation. Use of greater uncertainty factors was not necessary because the mechanism of irritation is not expected to differ between individuals. AEGL-1 values are given in Table 3.

| TABLE 3. AEGL-1 Values for Butyl Acrylate |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| 10-minute       | 30-minute       | 1-hour          | 4-hour          | 8-hour          |
| 8.3 ppm         | 8.3 ppm         | 8.3 ppm         | 8.3 ppm         | 8.3 ppm         |
| (44 mg/m³)      | (44 mg/m³)      | (44 mg/m³)      | (44 mg/m³)      | (44 mg/m³)      |

The reported odor threshold concentrations are not sufficiently qualified to derive a level of odor awareness (LOA) according to van Doorn et al. (2002).

6. DATA ANALYSIS FOR AEGL-2

6.1. Summary of Human Data Relevant to AEGL-2

Data in humans relevant to derivation of AEGL-2 values were not found.

6.2. Summary of Animal Data Relevant to AEGL-2

The best animal data relevant to derivation of AEGL-2 are from the subchronic study in which male and female Sprague-Dawley rats (n = 20) were exposed to 0, 21, 108, 211, or 546 ppm BA for 6 hours/day, 5 days/week, for 13 weeks (Klimisch et al. 1978). At the highest concentration, mortality, reduced body weight gain, and clinical signs of bloody ocular and nasal discharges and rhinitis were observed; marked lesions of the respiratory tract were found at necropsy. At 211 ppm all animals survived but had reduced body weight gain and showed bloody ocular and nasal discharges; slight edema and erosion of the nasal mucosa were observed.
histologically in a few individuals. Slight decreases in weight gain but no histopathological changes were observed in animals exposed to 108 ppm. The NOAEL was 21 ppm.

No maternal or developmental toxicity was seen in rats repeatedly exposed to 25 or 100 ppm during gestation (Rohm and Haas Co. 1992; Merkle and Klimisch 1983; Saillenfait et al. 1999).

### 6.3. Derivation of AEGL-2

The subchronic study by Klimisch et al. (1978) was used to derive AEGL-2 values. Repeated exposure to a concentration of 211 ppm for 6 hours/day resulted in clinical signs of toxicity including nasal irritation but no mortality. Slight lesions of the nasal mucosa were seen histologically. Values were scaled using the equation $C^n \times t = k$ where $n$ ranges from 0.8 to 3.5 (ten Berge et al. 1986). In the absence of an empirically derived, chemical-specific exponent, scaling was performed using $n = 3$ for extrapolating to the 30-minute and 1- and 4-hour time points and $n = 1$ for the 8-hour time point. A total uncertainty factor of 3 was used including 1 for interspecies extrapolation and 3 for intraspecies extrapolation. Use of greater uncertainty factors was not necessary because the mechanism of irritation is not expected to differ between individuals. According to Section 2.7 of the Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals (NRC 2001), 10-minute values are not to be scaled from an experimental exposure time of $\leq 4$ hours. Therefore, the 30-minute AEGL-2 value was also adopted as the 10-minute value. AEGL-2 values are given in Table 4.

<table>
<thead>
<tr>
<th>TABLE 4. AEGL-2 Values for Butyl Acrylate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>10-minute</strong></td>
</tr>
<tr>
<td>160 ppm</td>
</tr>
<tr>
<td>(850 mg/m³)</td>
</tr>
</tbody>
</table>

### 7. DATA ANALYSIS FOR AEGL-3

#### 7.1. Summary of Human Data Relevant to AEGL-3

Human exposure data relevant to derivation of AEGL-3 values were not available. No reports of human lethality from exposure to EA were found in the literature.

#### 7.2. Summary of Animal Data Relevant to AEGL-3

The best animal data relevant to derivation of AEGL-3 values is the Oberly and Tansy (1985) 4-hour $L_{C50}$ study in rats. This was a well conducted study with a wide range of analytically determined exposure concentrations. Clinical signs of irritation were observed in animals during exposure and death was attributed to cardiopulmonary collapse. The calculated 4-hour $L_{C50}$ value was 2730 ppm.
Other studies reporting 4-hour LC₅₀ values in rats (BASF 1979b,c, 1980) are in good agreement with that of Oberly and Tansy (1985). These are also well conducted studies but lacked details of the experimental procedures.

7.3. Derivation of AEGL-3

The LC₅₀ study by Oberly and Tansy (1985) was well conducted and included mortality ratios at all concentrations. From these data a 4-hour BMCL₀₅ value was calculated by a log-probit analysis using US EPA Benchmark Dose Software version 1.3.2. The resulting 4-hour BMCL₀₅ of 1652 ppm was used to derive the 30-minute, and 1-, 4- and 8-hour AEGL-3 values. Values were scaled using the equation Cⁿ × t = k where n ranges from 0.8 to 3.5 (ten Berge et al. 1986). A value of n = 1.3 was calculated by combining 1- and 4-hour LC₅₀ data sets from ethyl acrylate (NAC 2004a) in a 3-dimensional probit analysis (Zwart et al. 1992). Use of an n value calculated from a structurally related chemical was considered appropriate because the mechanism leading to death is similar for both compounds. A total uncertainty factor of 10 was used including 3 for interspecies extrapolation and 3 for intraspecies extrapolation. Use of greater uncertainty factors was not necessary because the mechanism of toxicity (local damage in the lower airways/lungs) is not expected to differ between individuals. According to Section 2.7 of the Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals (NRC 2001), 10-minute values are not to be scaled from an experimental exposure time of ≥4 hours. Therefore, the 30-minute AEGL-3 value was also adopted as the 10-minute value. AEGL-3 values are given in Table 5.

<table>
<thead>
<tr>
<th>TABLE 5. AEGL-3 Values for Butyl Acrylate</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-minute</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>820 ppm (4400 mg/m³)</td>
</tr>
</tbody>
</table>

8. SUMMARY OF AEGLS

8.1. AEGL Values and Toxicity Endpoints

The derived AEGL values for various levels of effects and durations of exposure are summarized in Table 6. AEGL-1 was based on a no-effect level for sensory irritation in rats. AEGL-2 values were derived from a subchronic study resulting in clinical signs and microscopic lesions of the nasal mucosa. The basis for AEGL-3 was a calculated 4-hour BMCL₀₅ from lethality data in the rat.
### TABLE 6. Summary of AEGL Values

<table>
<thead>
<tr>
<th>Classification</th>
<th>Exposure Duration</th>
<th>10-minute</th>
<th>30-minute</th>
<th>1-hour</th>
<th>4-hour</th>
<th>8-hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEGL-1 (Nondisabling)</td>
<td></td>
<td>8.3 ppm</td>
<td>8.3 ppm</td>
<td>8.3 ppm</td>
<td>8.3 ppm</td>
<td>8.3 ppm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(44 mg/m³)</td>
<td>(44 mg/m³)</td>
<td>(44 mg/m³)</td>
<td>(44 mg/m³)</td>
<td>(44 mg/m³)</td>
</tr>
<tr>
<td>AEGL-2 (Disabling)</td>
<td></td>
<td>160 ppm</td>
<td>160 ppm</td>
<td>130 ppm</td>
<td>81 ppm</td>
<td>53 ppm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(850 mg/m³)</td>
<td>(850 mg/m³)</td>
<td>(690 mg/m³)</td>
<td>(430 mg/m³)</td>
<td>(280 mg/m³)</td>
</tr>
<tr>
<td>AEGL-3 (Lethal)</td>
<td></td>
<td>820 ppm</td>
<td>820 ppm</td>
<td>480 ppm</td>
<td>170 ppm</td>
<td>97 ppm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(4400 mg/m³)</td>
<td>(4400 mg/m³)</td>
<td>(2600 mg/m³)</td>
<td>(906 mg/m³)</td>
<td>(520 mg/m³)</td>
</tr>
</tbody>
</table>

### 8.2. Comparison with Other Standards and Guidelines

Standards and guidance levels for workplace and community exposures are listed in Table 7. The ACGIH recommends a TLV of 2 ppm for workers (ACGIH 2003) while the NIOSH REL is 10 ppm (NIOSH, 2003). A NIOSH IDLH has not been established. ERPG-3 and -2 values were based on no effect levels for lethality and developmental toxicity effects and the ERPG-1 is at or below a moderate odor intensity level (AIHA 1995b). The occupational exposure limits from ACGIH, Germany, The Netherlands, and Sweden are 2-10 ppm.
### TABLE 7. Extant Standards and Guidelines for Butyl Acrylate

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Exposure Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10 minute</td>
</tr>
<tr>
<td>AEGL-1</td>
<td>8.3 ppm</td>
</tr>
<tr>
<td>AEGL-2</td>
<td>160 ppm</td>
</tr>
<tr>
<td>AEGL-3</td>
<td>820 ppm</td>
</tr>
<tr>
<td>ERPG-1 (AIHA)</td>
<td></td>
</tr>
<tr>
<td>ERPG-2 (AIHA)</td>
<td></td>
</tr>
<tr>
<td>ERPG-3 (AIHA)</td>
<td></td>
</tr>
<tr>
<td>REL-TWA (NIOSH)</td>
<td></td>
</tr>
<tr>
<td>TLV-TWA (ACGIH)</td>
<td></td>
</tr>
<tr>
<td>MAK (Germany)</td>
<td></td>
</tr>
<tr>
<td>MAK Peak Limit (Germany)</td>
<td></td>
</tr>
<tr>
<td>MAC (The Netherlands)</td>
<td></td>
</tr>
<tr>
<td>OEL-TWA (Sweden)</td>
<td></td>
</tr>
<tr>
<td>OEL-STEL (Sweden)</td>
<td></td>
</tr>
</tbody>
</table>

*ERPG (Emergency Response Planning Guidelines, American Industrial Hygiene Association (AIHA 1995b, 2003)*

The ERPG-1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed for up to one hour without experiencing other than mild, transient adverse health effects or without perceiving a clearly defined objectionable odor.

The ERPG-2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed for up to one hour without experiencing or developing irreversible or other serious health effects or symptoms that could impair an individual’s ability to take protection action.

The ERPG-3 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed for up to one hour without experiencing or developing life-threatening health effects.

*NIOSH REL-TWA (National Institute of Occupational Safety and Health, Recommended Exposure Limits - Time Weighted Average) (NIOSH 2003) is defined analogous to the ACGIH-TLV-TWA.*

*ACGIH TLV-TWA (American Conference of Governmental Industrial Hygienists, Threshold Limit Value – Time Weighted Average) (ACGIH 2003) is the time-weighted average concentration for a normal 8-hour workday and a 40-hour workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect. SEN:sensitizer*

*MAK (Maximale Arbeitsplatzkonzentration [Maximum Workplace Concentration]) (Deutsche Forschungsgemeinschaft [German Research Association] 2002) is defined analogous to the ACGIH-TLV-TWA. “Sh” designates substances which can cause allergic reactions of the skin and mucosa.*
8. MAK Spitzenbegrenzung (Peak Limit \([I(2)]\)) (German Research Association 2002)

constitutes the maximum average concentration to which workers can be exposed for a period up to 15 minutes with no more than 4 exposure periods per work shift; total exposure may not exceed 8-hour MAK.

9. MAC (Maximaal Aanvaaraarde Concentratie [Maximal Accepted Concentration]) (SDU Uitgevers [under the auspices of the Ministry of Social Affairs and Employment], The Hague, The Netherlands 2000) is defined analogous to the ACGIH-TLV-TWA.

10. OEL-TWA (Occupational Exposure Limits - Time-weighted-average) (IPCS 2003) is an occupational exposure limit value for exposure during one working day.

11. OEL-STEL (Occupational Exposure Limits - Short-term exposure limit) (IPCS 2003) is an occupational exposure limit value for exposure during a reference period of fifteen minutes.

8.3. Data Adequacy and Research Needs

No human data were available. Worker monitoring studies did not report potential individual exposure or effects. No animal data which matched the definition of AEGL-2 were available. However, AEGL-3 values were based on a well-conducted study with adequate information.

9. REFERENCES


BASF.  1979e.  Bericht über die bestimmung der akuten inhalationstoxizität LC\(_{50}\) von n-butylacrylat bie 4stüdiger exposition an NMRI-mäusen (nüchtern).  BASF, Gewerbehygiene und Toxikologie, kli-br 14.02.79.

BASF.  1980.  Bestimmung der akuten inhalationstoxizität LC\(_{50}\) von butylacrylat als dampf bie 4stüdiger exposition an Sprague-Dawley-ratten.  BASF, Gewerbehygiene und Toxikologie, kli-br 01.02.80.
n-BUTYL ACRYLATE


Rohm and Haas, Co. 1988. Olfactory function in chemical workers exposed to acrylate and methacrylate vapors with attachments, cover sheets and letters dated 031488 and 081089 (sanitized). Doc. ID 86-890001519S.


APPENDIX A: Derivation of AEGL Values
**Derivation of AEGL-1**

- **Key Studies:** Rohm and Haas Co. 1992; Merkle and Klimisch 1983
- **Toxicity endpoint:** No fetal effects and no clinical signs of toxicity in dams exposed to 25 ppm, 6 hours/day on gestation days 6-15.
- **Time scaling:** None
- **Uncertainty factors:** 3 (1 for intraspecies variability and 3 for interspecies variability)
- **Modifying factor:** None
- **Calculations:** \( \frac{C}{UFs} = \frac{25 \text{ ppm}}{3} = 8.3 \text{ ppm} \)
- **10-minute AEGL-1:** 8.3 ppm
- **30-minute AEGL-1:** 8.3 ppm
- **1-hour AEGL-1:** 8.3 ppm
- **4-hour AEGL-1:** 8.3 ppm
- **8-hour AEGL-1:** 8.3 ppm
Derivation of AEGL-2

Key Studies: Klimisch et al. 1978

Toxicity endpoints: A concentration of 211 ppm for 6 h/d, 5 d/week, for 13 weeks resulted in clinical signs of toxicity and microscopic lesions of the nasal mucosa.

Time scaling: $C^n \times t = k$ (ten Berge et al. 1986)
n = 3 for extrapolating to the 30-min and 1- and 4-hour time points; n = 1 for extrapolating to the 8-hr time point

Uncertainty factors: 3 (3 for intraspecies variability and 1 for interspecies variability)

Modifying factor: None

Calculations:

30-min and 1- and 4-hr time points

$\left( \frac{C}{UFs} \right)^3 \times t = k$

$(211 \text{ ppm}/3)^3 \times 6 \text{ hr} = 2.088 \times 10^6 \text{ ppm}^3\cdot\text{hr}$

8-hr time point

$\left( \frac{C}{UFs} \right)^1 \times t = k$

$(211 \text{ ppm}/3)^1 \times 6 \text{ hr} = 422 \text{ ppm}^1\cdot\text{hr}$

10-minute AEGL-2: 160 ppm

30-minute AEGL-2: $(2.088 \times 10^6 \text{ ppm}^3\cdot\text{hr}/0.5 \text{ hr}) = 160 \text{ ppm}$

1-hour AEGL-2: $(2.088 \times 10^6 \text{ ppm}^3\cdot\text{hr}/1 \text{ hr}) = 130 \text{ ppm}$

4-hour AEGL-2: $(2.088 \times 10^6 \text{ ppm}^3\cdot\text{hr}/4 \text{ hr}) = 81 \text{ ppm}$

8-hour AEGL-2: $(422 \text{ ppm}^1\cdot\text{hr}/8) = 53 \text{ ppm}$
Derivation of AEGL-3

Key Study: Oberly and Tansy 1985

Toxicity endpoint: The 4-hour LC₅₀ value of 2730 ppm in rats was used for derivation of AEGL-3 values. From these data, a 4-hour BMCL₀₅ value was calculated by a log-probit analysis. The resulting 4-hour BMCL₀₅ of 1652 ppm was used to derive the 30-minute, 1-hour, 4-hour, and 8-hour AEGL-3 values.

Time scaling \( C^n \times t = k \) (ten Berge et al. 1986)
\[ n = 1.3; \text{ calculated by combining 1- and 4- hour LC}_{50} \text{ data sets from ethyl acrylate (NAC 2004a) in a 3-dimensional probit analysis (Zwart et al. 1992)} \]

Uncertainty factors: 10 (3 for intraspecies variability and 3 for interspecies variability)

Modifying factor: None

Calculations:
\[ (C/UFs)^{1.3} \times t = k \]
\[ (1652 \text{ ppm/10})^{1.3} \times 4 \text{ hr} = 3058 \text{ ppm}^{1.3}\text{ hr} \]

10-minute AEGL-3: 820 ppm

30-minute AEGL-3: \( (3058 \text{ ppm}^{1.3}\text{ hr/0.5 hr}) = 820 \text{ ppm} \)

1-hour AEGL-3: \( (3058 \text{ ppm}^{1.3}\text{ hr/1 hr}) = 480 \text{ ppm} \)

4-hour AEGL-3: \( (3058 \text{ ppm}^{1.3}\text{ hr/4 hr}) = 170 \text{ ppm} \)

8-hour AEGL-3: \( (3058 \text{ ppm}^{1.3}\text{ hr/8 hr}) = 97 \text{ ppm} \)
APPENDIX B: Benchmark Calculations
Benchmark Calculations

The benchmark calculations are based on the study by Oberly and Tansy (1985) using a range of five concentrations in rats to determine a 4-hour LC$_{50}$. For the derivation of AEGL-3, a BMCL$_{05}$ of 1652 ppm, derived with the Log-Probit model, was used.

BMCL$_{05} = 1652$ ppm
BMC$_{01} = 1775$ ppm
Dependent variable = Mortality
Independent variable = Conc.
Slope parameter is not restricted

Total number of observations = 6
Total number of records with missing values = 0
Maximum number of iterations = 250
Relative Function Convergence has been set to: 1e-008
Parameter Convergence has been set to: 1e-008

User has chosen the log transformed model

Default Initial (and Specified) Parameter Values
  background = 0
  intercept = -37.3048
  slope = 4.7058

Asymptotic Correlation Matrix of Parameter Estimates
(*** The model parameter(s) -background have been estimated at a boundary point, or have been specified by the user, and do not appear in the correlation matrix)

<table>
<thead>
<tr>
<th></th>
<th>intercept</th>
<th>slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>intercept</td>
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<td>-1</td>
</tr>
<tr>
<td>slope</td>
<td>-1</td>
<td>1</td>
</tr>
</tbody>
</table>

Parameter Estimates

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>Std. Err.</th>
</tr>
</thead>
<tbody>
<tr>
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<td>NA</td>
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<tr>
<td>intercept</td>
<td>-41.1086</td>
<td>11.4106</td>
</tr>
<tr>
<td>slope</td>
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<td>1.44983</td>
</tr>
</tbody>
</table>

NA - Indicates that this parameter has hit a bound implied by some inequality constraint and thus has no standard error.
Analysis of Deviance Table

<table>
<thead>
<tr>
<th>Model</th>
<th>Log(likelihood)</th>
<th>Deviance</th>
<th>Test DF</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full model</td>
<td>-22.3996</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fitted model</td>
<td>-23.0385</td>
<td>1.27778</td>
<td>4</td>
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</tr>
<tr>
<td>Reduced model</td>
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<td>24.7906</td>
<td>5</td>
<td>0.0001529</td>
</tr>
</tbody>
</table>

AIC: 50.077

Goodness of Fit

<table>
<thead>
<tr>
<th>Dose</th>
<th>Est. Prob.</th>
<th>Expected</th>
<th>Observed</th>
<th>Size</th>
<th>Scaled Residual</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0000</td>
<td>0.0000</td>
<td>0.0000</td>
<td>0</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>1990.00</td>
<td>0.0416</td>
<td>0.416</td>
<td>0</td>
<td>10</td>
<td>-0.6588</td>
</tr>
<tr>
<td>2035.00</td>
<td>0.0530</td>
<td>0.530</td>
<td>1</td>
<td>10</td>
<td>0.6636</td>
</tr>
<tr>
<td>2500.00</td>
<td>0.2913</td>
<td>2.913</td>
<td>3</td>
<td>10</td>
<td>0.06083</td>
</tr>
<tr>
<td>2828.00</td>
<td>0.5356</td>
<td>5.356</td>
<td>5</td>
<td>10</td>
<td>-0.2257</td>
</tr>
<tr>
<td>3041.00</td>
<td>0.6793</td>
<td>6.793</td>
<td>7</td>
<td>10</td>
<td>0.1401</td>
</tr>
</tbody>
</table>

Chi-square = 0.95  DF = 4  P-value = 0.9175

Benchmark Dose Computation

Specified effect = 0.05
Risk Type = Extra risk
Confidence level = 0.95

BMC = 2023.91
BMDL = 1651.9
APPENDIX C: Derivation Summary for Butyl Acrylate AEGLs
ACUTE EXPOSURE GUIDELINE LEVELS FOR
n-BUTYL ACRYLATE (CAS Reg. No. 141-32-5)
DERIVATION SUMMARY

<table>
<thead>
<tr>
<th>AEGL-1 VALUES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>10-minute</td>
</tr>
<tr>
<td>8.3 ppm</td>
</tr>
</tbody>
</table>

Key Reference:

Test Species/Strain/Number: Rat/Sprague-Dawley/30
Exposure Route/Concentrations/Durations: Inhalation: 25-250 ppm, 6 hr/day, gestation days 6-15.
Effects:
25 ppm: no maternal effects or clinical signs.
135 and 250 ppm: decreased maternal body weight, clinical signs of irritation, reduced number of live fetuses and increased resorptions.
Endpoint/Concentration/Rationale: No-observed-effect level/25 ppm/below threshold for clinical signs.
Uncertainty Factors/Rationale:
Total uncertainty factor: 3
Interspecies: 1, clinical signs similar among different species.
Intraspecies: 3, mechanism of irritation is not expected to differ between individuals.
Modifying Factor: None
Animal to Human Dosimetric Adjustment: Not applicable
Time Scaling: Extrapolation to time points was not done.
Data Adequacy: No human data and only limited animal data were available.
### AEGL-2 VALUES

<table>
<thead>
<tr>
<th></th>
<th>10-minute</th>
<th>30-minute</th>
<th>1-hour</th>
<th>4-hour</th>
<th>8-hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration</td>
<td>160 ppm</td>
<td>160 ppm</td>
<td>130 ppm</td>
<td>81 ppm</td>
<td>53 ppm</td>
</tr>
</tbody>
</table>


Test Species/Strain/Number: Rat/Sprague-Dawley/20/sex/group

Exposure Route/Concentrations/Durations: Inhalation/ 0, 21, 108, 211, or 546 ppm/6 hr/day, 5 d/week, 13 weeks.

Effects: 21 ppm: NOAEL
108 ppm: decreased weight gain
211 ppm: decreased weight gain, clinical signs, lesions on nasal mucosa
546 ppm: mortality, decreased weight gain, clinical signs, lesions on nasal mucosa and necrosis of lungs

Endpoint/Concentration/Rationale: Clinical signs and histopathology/211 ppm/definition of AEGL-2.

Uncertainty Factors/Rationale:
- Total uncertainty factor: 3
  - Interspecies: 1, clinical signs similar among different species.
  - Intraspecies: 3, mechanism of irritation is not expected to differ between individuals.

Modifying Factor: None

Animal to Human Dosimetric Adjustment: Not applicable

Time Scaling: $C^n \times t = k$ where $n$ ranges from 0.8 to 3.5 (ten Berge et al. 1986). In the absence of an empirically derived, chemical-specific exponent, scaling was performed using $n = 3$ for extrapolating to the 30-minute and 1- and 4-hour time points and $n = 1$ for the 8-hour time point. According to Section 2.7 of the Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals (NRC 2001), 10-minute values are not to be scaled from an experimental exposure time of ≥4 hours. Therefore, the 30-minute AEGL-2 value was also adopted as the 10-minute value.

Data Adequacy: No acute exposure data were available for derivation of AEGL-2; values were derived from a subchronic study.
### AEGL-3 VALUES

<table>
<thead>
<tr>
<th></th>
<th>10-minute</th>
<th>30-minute</th>
<th>1-hour</th>
<th>4-hour</th>
<th>8-hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration (ppm)</td>
<td>820 ppm</td>
<td>820 ppm</td>
<td>480 ppm</td>
<td>170 ppm</td>
<td>97 ppm</td>
</tr>
</tbody>
</table>


**Test Species/Strain/Number:** Rat/Sprague-Dawley/10

**Exposure Route/Concentrations/Durations:** Inhalation/1990, 2035, 2500, 2828, or 3041 ppm/4 hr.

**Effects:**
2730 ppm: 4-hour LC50
Clinical signs of irritation during exposures; death due to cardiopulmonary collapse.

**Endpoint/Concentration/Rationale:** A 4-hour BMCL05 value was calculated by a log-probit analysis. The resulting 4-hour BMCL05 of 1652 ppm was used to derive the 10-minute, 30-minute, 1-hour, and 8-hour AEGL-3 values.

**Uncertainty Factors/Rationale:**
- Total uncertainty factor: 10
- Interspecies: 3, little species variation.
- Intraspecies: 3, mechanism of lethality is not expected to differ between individuals.

**Modifying Factor:** None

**Animal to Human Dosimetric Adjustment:** Not applicable

**Time Scaling:** \( C^n \times t = k \) where \( n \) ranges from 0.8 to 3.5 (ten Berge et al. 1986). A value of \( n = 1.3 \) was calculated by combining 1- and 4- hour LC50 data sets from ethyl acrylate (NAC 2004a) in a 3-dimensional probit analysis (Zwart et al. 1992). According to Section 2.7 of the Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals (NRC 2001), 10-minute values are not to be scaled from an experimental exposure time of \( \geq 4 \) hours. Therefore, the 30-minute AEGL-3 value was also adopted as the 10-minute value.

**Data Adequacy:** The key LC50 study was well conducted and included mortality ratios at all concentrations. Other studies reporting 4-hour LC50 values in rats (BASF 1979b,c, 1980) are in good agreement with that of Oberly and Tansy (1985).
APPENDIX D: Time-scaling Category Plot for Butyl Acrylate
No effect = No effect or mild discomfort
Discomfort = Notable transient discomfort/irritation consistent with AEGL-1 level effects
Disabling = Irreversible/long lasting effects or an impaired ability to escape
Some lethality = Some, but not all, exposed animals died
Lethal = All exposed animals died