n-Butyl Acetate

CAS Registry Number: 123-86-4

Prepared by

Jong-Song Lee, Ph.D.

Toxicology Division

Office of the Executive Director

TEXAS COMMISSION ON ENVIRONMENTAL QUALITY

Revision History

Original Development Support Document (DSD) posted as final on December 29, 2010.

Revised DSD March 14, 2014: The DSD was revised based on updated guidance in USEPA (2012). Default dosimetric adjustments from animal-to-human exposure for n-BA was conducted as a Category 1 vapor based on updated animal-to-human dosimetric recommendations in USEPA (2012). The default regional gas dose ratio for the extrathoracic region ($RGDR_{ET}$) is 1.

Revised DSD September 14, 2015: An odor-based value was not developed because n-butyl acetate does not have a pungent or disagreeable odor (TCEQ 2015). n-Butyl acetate has a sweet, sharp and fruity odor.

TABLE OF CONTENTS

n-Butyl Acetate
Page iii

LIST OF TABLES

List of Acronyms and Abbreviations

Abbreviation	Definition
AEGL	Acute Exposure Guideline Level
^{0} C	degrees centigrade
CNS	central nervous system
DSD	development support document
ET	extrathoracic
ESL	Effects Screening Level
^{acute}ESL	acute health-based Effects Screening Level for chemicals meeting minimum database requirements
^{acute}ESL$_{generic}$	acute health-based Effects Screening Level for chemicals not meeting minimum database requirements
^{acute}ESL$_{odor}$	acute odor-based Effects Screening Level
^{acute}ESL$_{veg}$	acute vegetation-based Effects Screening Level
^{chronic}ESL $_{nonthresholdr(c)}$	chronic health-based Effects Screening Level for nonthreshold (linear) dose response cancer effect
^{chronic}ESL $_{nonthreshold(nc)}$	chronic health-based Effects Screening Level for nonthreshold (linear) dose response noncancer effects
^{chronic}ESL$_{threshold(c)}$	chronic health-based Effects Screening Level for threshold (nonlinear) dose response cancer effects
^{chronic}ESL$_{threshold(nc)}$	chronic health-based Effects Screening Level for threshold (nonlinear) dose response noncancer effects
^{chronic}ESL$_{veg}$	chronic vegetation-based Effects Screening Level
F	exposure frequency, days per week
FOB	Functional observational battery
GD	gestation day
h	hour
$H_{b/g}$	blood:gas partition coefficient
$(H_{b/g})_A$	blood:gas partition coefficient, animal
$(H_{b/g})_H$	blood:gas partition coefficient, human
Hg	mercury
HEC	human equivalent concentration
HQ	hazard quotient
kg	kilogram

Abbreviation	Definition
LOAEL	lowest-observed-adverse-effect-level
MW	molecular weight
µg	microgram
µg/m^3	micrograms per cubic meter
mg	milligrams
mg/m^3	milligrams per cubic meter
min	minute
MOA	mode of action
n	number
NAC	National Advisory Committee
n-BA	n-butyl acetate
NOAEL	no-observed-adverse-effect-level
NOEL	no-observed-effect-level
POD	point of departure
POD$_{ADJ}$	point of departure adjusted for exposure duration
POD$_{HEC}$	point of departure adjusted for human equivalent concentration
ppb	parts per billion
ppm	parts per million
ReV	reference value
RGDR$_{ET}$	regional gas dose ratio extrathoracic region
SA$_{ET}$	surface area extrathoracic region
SCOB	scheduled-controlled operant behavior
SD	Sprague-Dawley
TCEQ	Texas Commission on Environmental Quality
TD	Toxicology Division
UF	uncertainty factor
UF$_H$	interindividual or intraspecies human uncertainty factor
UF$_A$	animal to human uncertainty factor
UF$_{Sub}$	subchronic to chronic exposure uncertainty factor
UF$_L$	LOAEL to NOAEL uncertainty factor
UF$_D$	incomplete database uncertainty factor
USEPA	United States Environmental Protection Agency

Abbreviation	Definition
V_E	minute volume

Chapter 1 Summary Tables

Table 1 for air monitoring and Table 2 for air permitting provide a summary of health- and welfare-based values from an acute and chronic evaluation of n-butyl acetate (n-BA). Please refer to Section 1.6.2 of the TCEQ Guidelines to Develop Toxicity Factors (TCEQ 2012) for an explanation of air monitoring comparison values (AMCVs), reference values (ReVs) and effects screening levels (ESLs) used for review of ambient air monitoring data and air permitting. Table 3 provides summary information on n-BA's physical/chemical data.

Table 1 Air Monitoring Comparison Values (AMCVs) for Ambient Air [a]

Short-Term Values	Concentration	Notes
Acute ReV	35,000 µg/m^3 (7,400 ppb) **Short-Term Health**	**Critical Effect(s):** eye, nose and throat irritation in male and female volunteers
$^{acute}ESL_{odor}$	---	Sweet, sharp and fruity odor
$^{acute}ESL_{veg}$	--- **Short-Term Vegetation**	No data found
Long-Term Values	**Concentration**	**Notes**
Chronic ReV	4,700 µg/m^3 (990 ppb) **Long-Term Health**	**Critical Effect(s):** minimal to mild necrosis of the olfactory epithelium, and decreased transient motor activity, decreased growth in rats
$^{chronic}ESL_{nonthreshold(c)}$	---	No data found
$^{chronic}ESL_{veg}$	--- **Long-Term Vegetation**	No data found

[a] n-BA is not monitored for by the TCEQ's ambient air monitoring program, so currently no ambient air data (i.e., peaks, annual averages, trends, etc.) are available to assess n-BA's concentrations in Texas ambient air.
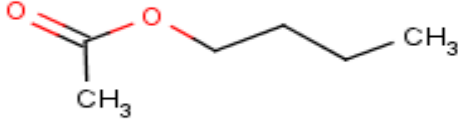
Table 2 Air Permitting Effects Screening Levels (ESLs)

Short-Term Values	Concentration	Notes
$^{acute}ESL$ (HQ = 0.3)	11,000 μg/m^3 (2,200 ppb) [a] **Short-Term ESL for Air Permit Reviews**	**Critical Effect(s):** eye, nose and throat irritation in male and female volunteers
$^{acute}ESL_{odor}$	---	Sweet, sharp and fruity odor
$^{acute}ESL_{veg}$	---	No data found
Long-Term Values	**Concentration**	**Notes**
$^{chronic}ESL_{threshold(nc)}$ (HQ = 0.3)	1,400 μg/m^3 (300 ppb)[b] **Long-Term ESL for Air Permit Reviews**	**Critical Effect(s):** minimal to mild necrosis of the olfactory epithelium, and decreased transient motor activity, decreased growth in rats
$^{chronic}ESL_{nonthreshold(c)}$	---	No data found
$^{chronic}ESL_{veg}$	---	No data found

[a] Based on the acute ReV of 35,000 μg/m^3 (7,400 ppb) multiplied by 0.3 to account for cumulative and aggregate risk during the air permit review.

[b] Based on the chronic ReV of 4,700 μg/m^3 (990 ppb) multiplied by 0.3 to account for cumulative and aggregate risk during the air permit review.

Table 3 Chemical and Physical Data

Parameter	Value	Reference
Molecular Formula	C_6-H_{12}-O_2	ChemIDplus
Chemical Structure		ChemIDplus
Molecular Weight	116.16	ACGIH 2001
Physical State	Flammable liquid	ACGIH 2001
Color	Colorless	ACGIH 2001
Odor	Fruity odor, sharp and sweet	ACGIH 2001
CAS Registry Number	123-86-4	ChemIDplus
Synonyms	1-butyl acetate, acetic acid n-butyl ester, butyl ethanoate	ChemIDplus
Solubility in water	8,400 mg/L at 25^oC	ChemIDplus
Log P_{ow}	1.78	ChemIDplus
Vapor Pressure	11.5 mm Hg at 25^oC	ChemIDplus
Relative Vapor Density (air = 1) Relative	4.0	ACGIH 2001
Density (water = 1)	0.8826 at 20^oC	ACGIH 2001
Henry's Law Constant	2.81E-04 atm-m^3/mole	ChemIDplus
Melting Point	-78 ^{o}C	ChemIDplus
Boiling Point	126.1 ^{o}C	ChemIDplus
Conversion Factors	1 $\mu g/m^3$ = 0.21 ppb 1 ppb = 4.75 $\mu g/m^3$ at 25^oC	ACGIH 2001

Chapter 2 Major Uses or Sources

n-BA occurs naturally in bananas and related fruits and is produced and emitted during fermentation. It has also been found in a wide variety of food products. n-BA is mainly used as a solvent and a thinner in the production of nitrocellulose lacquers in the protective coatings industry. It is also used in the manufacturing of high-polish lacquers and varnishes, photographic film, nail polish removers, perfumes, oils, fats, vinyl resins, waxes, and camphor. n-BA is also used in the preservation of foodstuffs and in the inks and thinners of printing processes (ACGIH 2001, DECOS 2001, IPCS 2005).

n-BA can be released into the air from industrial plants during the manufacturing process. n-BA is also released to the environment during its use in industrial coatings and use as a solvent in lacquers, inks, and adhesives. n-BA released to the environment is likely to volatilize to the atmosphere, where it will undergo photochemical oxidation reactions with hydroxyl radicals and chlorine atoms (IPCS 2005). Concentrations of 0.1 and 4.8 μg/m^3 resulting from emissions from United States industrial and chemical waste disposal sites have been reported (Pellizzari 1982, as cited in IPCS 2005).

Chapter 3 Acute Evaluation

3.1 Health-Based Acute ReV and ^{acute}ESL

n-BA is considered to have low toxicity. Acute exposures of animals to high concentrations of n-BA vapor are not usually toxic. A recent well designed and performed animal experiment indicated that the toxicity of n-BA vapor following a single 4-hour (h) inhalation is low, with no deaths occurring at exposures up to approximately 6,867 ppm (Norris et al. 1997).

Results of an animal toxicity study indicate that n-BA causes mild neurobehavioral toxicity and is, at most, only slightly irritating to the skin and eyes (CIREP 1989), whereas humans experienced minimal irritation to the eyes and respiratory tract, but central nervous system (CNS) effects and lung function were not affected (Iregren et al. 1993).

3.1.1 Physical/Chemical Properties

n-BA is a colorless, flammable liquid with a fruity, sweet and sharp odor (ACGIH 2001). It is soluble in water; and miscible with alcohol, ether, and organic solvents including hydrocarbons (ACGIH 2001). The main chemical and physical properties of n-BA are summarized in Table 3.

3.1.2 Key Human Study

The most common and primary acute adverse effect of exposure to n-BA in humans is irritation of the eyes, nose, throat, and mucous membranes. Sensitivity to odor occurs at concentrations several orders of magnitude lower than levels at which nose and throat irritation are reported (NIOSH 1978, DECOS 2001, IPCS 2005).

The study conducted by Iregren et al. (1993) was chosen as the sole key human study. In this study, local irritation and CNS effects of n-BA on 24 non-smoking human volunteers of both sexes without previous occupational solvent exposure were studied. Three inhalation experiments with different exposure levels (analytical concentrations) were reported:

1. four 20-minute (min) sessions, 24 h apart, with concentrations of 350, 700, 1,050, and 1,400 mg/m^3 (n = 24);
2. two 20-min sessions, 7 days apart, with concentrations of 70 (served as a control condition) and 1,400 mg/m^3 (n = 23); and
3. two 4-h exposures with a 7-day interval and exposure concentrations of 70 (served as a control condition) and 700 mg/m^3 (n = 12).

A 10-point rating scale (from 0 "not at all" to 9 "very much") for perceived irritation (eyes, throat, nose, skin, breathing difficulties, smell) and for CNS symptoms (headache, nausea, etc.) were measured in all three experiments. Various measures of eye irritation, and pulmonary function tests were also used in Experiments 2 and 3. The results showed that there were no significant changes in CNS symptoms in any of the three experiments, and in lung function in either Experiments 2 or 3.

In Experiment 1, changes in categorical rating of irritation from baseline level before exposure were not significant for any of the items rated. Although the authors indicated that there were tendencies toward a difference, with borderline statistical significance for the "Irritation to the throat" and "Difficult to breathe" items. For these items, there was a monotonous increase in ratings with higher exposure levels. However, most subjects used only the lower ranges of the ten-point rating scales. The exposure level of 1,400 mg/m^3 was considered a lowest-observed-adverse-effects level (LOAEL) for category scales measuring irritation, although the results indicate only weak irritation effects from the 20-min exposures.

In Experiments 2 and 3, the results showed only a very low level of irritation but significant difference between the control and the exposure condition as revealed by categorical ratings (mean ratings were at the extreme lower part of the scale), magnitude estimation, and some of the clinical measures of eye irritation and pulmonary functions, such as eye redness, lipid layer thickness, and bronchial responsiveness. Exposure to the highest concentrations tested (i.e., 1,400 mg/m^3 for 20 min from Experiment 2; and 700 mg/m^3 for 4 h from Experiment 3) caused only minimal irritation to the eyes and respiratory tract. The authors noted that all of the subjects rated n-BA as a "very slight irritation" when rating on categorical scales. As shown in Figure 1 of the Iregren et al. (1993) study, the results from Experiments 2 and 3 indicated that, except for the ratings of sensation of a bad smell, exposure duration had no significant influence on other categorical rating items such as irritation to the eye, the nose, or the throat, and breathing difficulties. Thus, except for the sensation of a bad smell, local irritation effects caused by n-BA are concentration, but not duration, dependent. Sensory adaptation was observed at the 1,400 mg/m^3 exposure level in the 20-min exposure of Experiment 2, and both at the 70 and at the 700

mg/m^3 exposure level in the 4-h exposure of Experiment 3. The sensation of smell is addressed in Section 3.2.1 Odor Perception. A 20-min LOAEL of 1,400 mg/m^3 for local irritation was identified from Experiment 2. Additionally, a 4-h LOAEL of 700 mg/m^3 for minimal irritation to the eyes and respiratory tract was identified from Experiment 3. The 4-h LOAEL of 700 mg/m^3 ($\approx$ 150 ppm) is lower than the 20-min LOAEL of 1,400 mg/m^3 ($\approx$ 290 ppm), and thus was used as the point of departure (POD).

3.1.3 Human Supporting Study

In an inhalation study conducted by Nelson et al. (1943), 10 volunteer subjects of mixed sexes were exposed to n-BA vapor of 200 and 300 ppm (nominal concentrations) for 3-5 min. After the exposure, each individual classified the effects on the eyes, nose, and throat. The degree of irritation was scored subjectively based on the three categories "no reaction," "slightly irritating," and "very irritating." The majority reported exposure to approximately 200 ppm for 3-5 min to be irritating to the throat and exposure to approximately 300 ppm to be irritating to the nose and the eyes (and very irritating to the throat). A freestanding LOAEL of 200 ppm for 3-5 min for irritation was identified from this study. Since an unexposed control group was not included and the exposure duration (3-5 min) was very short, the LOAEL was not used as the POD. The Toxicology Division (TD) believes the 20-min LOAEL of 1,400 ($\approx$ 290 ppm) mg/m³ and 4-h LOAEL of 700 mg/m^3 ($\approx$ 150 ppm) identified from the Iregren et al. (1993) study are more appropriate to use as the PODs (see Section 3.1.2) for derivation of a 1-h acute ReV and ESL.

3.1.4 Animal Supporting Studies

3.1.4.1 Bowen and Balster (1997)

Bowen and Balster (1997) investigated the neurobehavioral effects of inhaled n-BA in male mice. Five groups of 8 mice were exposed to 0, 1,000, 2,000, 4,000 and 8,000 ppm (nominal concentrations) for 20 min. Measurement of locomotor activity was monitored during the entire 20-min exposure session. The results showed that significant decreases in locomotor activity compared to control were observed at the highest concentrations examined (8,000 ppm). A 20-min LOAEL of 8,000 ppm ($\approx$ 38,000 mg/m^3) and no-observed-adverse-effect level (NOAEL) of 4,000 ppm ($\approx$ 19,000 mg/m^3) for neurobehavioral effects were identified from this study.

3.1.4.2 Bernard and David (1994 in DECOS 2001)

A study investigating effects on the CNS following acute exposure to n-BA vapor was conducted by Bernard and David (1994, as cited in DECOS 2001). Four groups of 20 Sprague-Dawley (SD) rats (10 per sex) were exposed to 0, 1,500, 3,000, 6,000 ppm (nominal concentrations) for 6 h. Motor activity measured in 10-min intervals during a 60-min period (30 min after ending exposure and on post-exposure days 1, 7, and 14) was transiently reduced (i.e., only immediately following exposure and not on post-exposure days 1–14) in the mid- and high-dose groups. The functional observational battery (FOB) examinations 1.5 h after ending exposure and on post-exposure days 7 and 14 showed no effects on motor activity in the open field. Effects were

observed directly after exposure only and included slightly unkempt hair coat in the high-dose group and increased forelimb grip strength for the female animals of the mid-dose group. A 6-h LOAEL of 3,000 ppm ($\approx$ 14,200 mg/m^3) and NOAEL of 1,500 ppm ($\approx$ 7,100 mg/m³) for CNS effects were identified from this study.

3.1.4.3 Bernard and David (1995 in DECOS 2001)

In an unpublished study conducted to select exposure concentrations for a subsequent 13-week study by Bernard and David (1995, as cited in DECOS 2001), male and female SD rats were exposed to n-BA vapor at approximately 0, 750, 1,500, or 3,000 ppm (nominal concentrations), 6 h/day, 5 days/week, for 2 weeks. Each exposure group consisted of 5 male and 5 female ad libitum-fed animals and 5 feed-restricted male animals. There were treatment-related reductions in activity levels (hypoactivity; slower response to tapping on the chamber wall). In the 750 ppm group, these reductions were of "minimal to minor" severity early in the exposure and absent by the end of the experiment. At 1,500 ppm, the severity of the effect decreased from "minor" to "minimal" over the course of the exposure, while in the 3,000 ppm exposed group, it remained "minor" throughout the experimental period. Other occasional signs noted were sialorrhoea (excessive saliva and drooling) in 4/15 and 8/15 animals at 1,500 ppm and 3,000 ppm, respectively, and red sialorrhoea, porphyrin tears and nasal discharge, brown discolored facial hair, and unkempt hair coat in individual animals of the 3,000 ppm group. There was no apparent difference in these clinical signs between ad libitum-fed and feed-restricted animals. A 2-week LOAEL of 1,500 ppm ($\approx$ 7,100 mg/m³) and NOAEL of 750 ppm ($\approx$ 3,560 mg/m³) for reductions in activity levels were identified from this study.

The LOAEL and/or NOAEL for CNS effects identified from the aforementioned three animal studies (Bowen and Balster (1997), Bernard and David (1994, 1995)) were relatively high compared to those observed for local irritation effects in humans, thus these LOAEL/NOAEL values were not used as the PODs. In addition, humans exposed to n-BA did not show signs of CNS effects at concentrations producing minimal irritation to the eyes and respiratory tract (Iregren et al. 1993).

3.1.5 Reproductive/Developmental Toxicity Studies

Reproductive and developmental toxicology were evaluated in rats and rabbits by Hackett et al. (1983), as cited in CIREP (1989) and DECOS (2001). Groups of 21-25 rabbits were exposed to 0 (group 1) or 1,500 ppm n-BA, 7 h/day, during gestation days (GD) 7-19 (group 2) or 1-19 (group 3). No effects were observed in the measurements for fertility and reproductive status in rabbits exposed to n-BA. Increased incidences in minor developmental effects including retinal folds (p = 0.04), misaligned sternebrae (p=0.04), and morphological variations in gallbladder (p = 0.05) were noticed in group 3. No significant malformations were observed in fetuses in any exposure groups.

Groups of 37-42 rats were exposed to filtered air (group 1) or 1,500 ppm, 7 h/day, during GD 7-16 (group 2), GD 1-16 (group 3), or pregestationally for 3 weeks (5 days/week) and subsequently during GD 1-16 (group 4). The animals of all groups were mated with unexposed males. Signs of minor developmental toxicity were observed. In all groups exposed to n-BA, fetal growth (body weight, crown–rump length) was statistically significantly reduced. Increased incidences of rib dysmorphology and reduced pelvic ossification were observed in group 2 ($p = 0.05$ and 0.08, respectively) or group 3 ($p = 0.07$ and 0.002, respectively) but not in group 4. In addition, there was an increased incidence of hydroureter in group 4 ($p = 0.05$). Mating and reproductive performance (pregnancy rates, numbers of corpora lutea, implantation sites, resorptions, live fetuses per litter) were not affected in group 4. The increase of rib dysmorphology might be an indicator of an effect of n-BA on development, however, since a similar increase was not observed in the group of rats exposed during this period of gestation subsequent to a pregestational exposure (group 4), the investigators concluded that n-BA was not teratogenic.

The LOAEL of 1,500 ppm for mild developmental toxicity in rats was relatively high compared to those observed for local irritation effects in humans, therefore it was not used as a POD, since protecting against the minimal irritation to the eyes and respiratory tract observed in humans after exposure to n-BA would protect against reproductive/developmental effects.

3.1.6 Mode of Action (MOA) Analysis and Dose Metric

n-BA is quickly hydrolyzed to acetic acid and n-butanol in the blood, liver, small intestine, and respiratory tract. It is probably excreted via exhaled air and urine both as the unchanged compound and as metabolites (butanol, butyraldehyde, and butyrate) after transformation in the body (IPCS 2005). Humans exposed to atmospheres containing n-BA at a concentration of 200 mg/m^3 were reported to excrete 50% of the inhaled compound in the exhaled air (DECOs 2001).

The MOA of n-BA for minimal irritation to the eyes and respiratory tract is not known, although the acetic acid metabolite may be involved. The acute local irritation effects are concentration dependent (see Section 3.1.2.1). The CNS effects during exposure of n-BA were likely produced by n-butanol or its metabolites (butyraldehyde or butyric acid) (David et al. 1998). Both irritation and CNS effects are assumed to have a threshold or nonlinear dose-response relationship.

Since the key study is based on human volunteers exposed to the parent chemical, and information on other more appropriate dose metrics were not available, exposure concentration of the parent chemical will be used as the dose metric.

3.1.7 Critical Effect and Dosimetric Adjustments

The 4-h LOAEL of 700 mg/m^3 for local irritation identified by Iregren et al. (1993) was used as the POD_{HEC} to derive the acute ReV and $^{acute}ESL$. As indicated in the Iregren et al. (1993) study, the local irritation effects of n-BA are only concentration dependent (see Section 3.1.2), so an exposure duration adjustment from 4 h to 1 h for the 4-h LOAEL was not conducted (TCEQ 2012). Thus, the 4-h LOAEL of 700 mg/m^3 was used as a 1-h concentration POD_{HEC}.

3.1.8 Adjustments of the POD$_{HEC}$

The MOA for mild irritant effects has a nonlinear (threshold) dose-response relationship. The acute ReV of 35 mg/m^3 or 35,000 μg/m^3 was derived by applying a total uncertainty factor (UF) of 20 to the POD$_{HEC}$ of 700 mg/m³:

- a UF$_H$ of 10 for human variability. The TCEQ believes that a UF$_H$ of 10 is sufficient to account for human variation including possible child/adult differences. There is no data that indicate that a UF$_H$ larger than 10 is needed to protect children or other sensitive sub groups

- a UF$_L$ of 2 for extrapolation from a LOAEL to a NOAEL, A low to moderate UF$_L$ of 2, based on the geometric mean (1.7, rounded to 2) of a UF$_L$ of 1 (NOAEL) and 3 (LOAEL for mild and transient effects), was used for extrapolation from a LOAEL to NOAEL because the irritation to the eyes and respiratory tract rated by all of the tested subjects was very minimal,

- a UF$_D$ of 1 for database uncertainty. A UF$_D$ of 1 was used for database uncertainty because the overall quality and numbers of the human and animal studies are high.

$$\text{Acute ReV} = \text{POD}_{ADJ} / (\text{UF}_H \times \text{UF}_L \times \text{UF}_D)$$
$$= 700 \text{ mg/m}^3 / (10 \times 2 \times 1)$$
$$= 35 \text{ mg/m}^3$$
$$= 35 \text{ mg/m}^3$$

Other UFs are not applicable (i.e., extrapolation from an animal-to-human study). Confidence is considered medium to high on the ReV derived from the 4-h inhalation LOAEL.

3.1.9 Health-Based Acute ReV and ^{acute}ESL

The ^{acute}ESL of 11,000 μg/m^3 (2,200 ppb) was based on the acute ReV of 35,000 μg/m^3 (7,400 ppb) (rounded to 2 significant figures) multiplied by a HQ of 0.3 and rounded to two significant figures at the end of all calculations (Table 4).

Table 4 Derivation of the Acute ReV and ^{acute}ESL

Parameter	Summary
Study	Iregren et al. 1993
Study Population	24 healthy male and female volunteers
Study Quality	Medium to high
Exposure Method	Exposure via inhalation at 70 and 700 mg/m^3
Critical Effects	Slight local irritation to eyes and respiratory tract
POD	700 mg/m^3 (LOAEL$_{[HEC]}$)
Exposure Duration	4 h
Extrapolation to 1 h (POD$_{ADJ}$)	700 mg/m^3
Total uncertainty factors (UFs)	20
Interspecies UF	N/A
Intraspecies UF	10
LOAEL-to-NOAEL UF	2
Incomplete Database UF	1
Database Quality	high
Acute ReV [1 h] **(HQ = 1)**	**35,000 μg/m^3 (7,400 ppb)**
^{acute}**ESL [1 h]** **(HQ = 0.3)**	**11,000 μg/m^3 (2,200 ppb)**

3.2 Welfare-Based Acute ESLs

3.2.1 Odor Perception

n-BA has a sweet and sharp odor that has been described as fruity. There have been several published odor threshold values listed below (Table 5). Since n-BA does not have a pungent or disagreeable odor, an $^{acute}ESL_{odor}$ was not developed (TCEQ 2015).

Table 5 n-Butyl Acetate Odor Threshold Values

Study	Odor Detection Value	Odor Recognition Value
van Harreveld et al. (2003)	361 $\mu g/m^3$ (76 ppb)	
van Doorn et al. (2001, 2002)	361 $\mu g/m^3$ (76 ppb)	
Nagata (2003)	76 $\mu g/m^3$ (16 ppb)	
Hellman and Small (1973, 1974)	29 $\mu g/m^3$ (6 ppb)	180 $\mu g/m^3$ (38 ppb)
May (1966)	35.2 mg/m^3 (7.4 ppm)	57 mg/m^3 (12 ppm)

3.2.2 Vegetation Effects

No information was found to indicate that special consideration should be given to possible vegetation effects from n-BA.

3.3 Short-Term ESL and Values for Air Monitoring Evaluation

This acute evaluation resulted in the derivation of the following acute values:

- acute ReV = 35,000 $\mu g/m^3$ (7,400 ppb)
- $^{acute}ESL$ = 11,000 $\mu g/m^3$ (2,200 ppb)

The acute ReV of 35,000 $\mu g/m^3$ (7,400 ppb) will be used for evaluation of ambient air monitoring data (Table 1). The short-term ESL for air permit evaluations is the $^{acute}ESL$ of 11,000 $\mu g/m^3$ (2,200 ppb) (Table 2). The health-based $^{acute}ESL$ (HQ = 0.3) is not used for evaluation of air monitoring data.

3.4 Acute Inhalation Observed Adverse Effect Level

The acute inhalation observed adverse effect level would be the LOAEL from the key human study (Iregren et al. 1993) of 700,000 $\mu g/m^3$ (150,000 ppb). The $LOAEL_{HEC}$ determined from human studies, where slight local irritation to eyes and respiratory tract occurred in some individuals, represents a concentration at which it is probable that similar effects could occur in some individuals exposed to this level over the same or longer durations as those used in the study. Importantly, effects are not a certainty due to potential intraspecies differences in sensitivity. The inhalation observed adverse effect level is provided for informational purposes

only (TCEQ 2012). As the basis for development of inhalation observed adverse effect levels is limited to available data, future studies could possibly identify a lower POD for this purpose.

The margin of exposure between the acute observed adverse effect level and the ReV is a factor of 20. (Table 4).

Chapter 4 Chronic Evaluation

4.1 Noncarcinogenic Potential

The major noncarcinogenic effects from repeated inhalation exposure to n-BA are neurological and local irritation effects. No chronic studies for systemic effects from chronic inhalation exposure of n-BA were reported. However, there are some subchronic inhalation studies of n-BA on neurotoxic effects in animals. The TD used subchronic exposure studies on neurotoxicity to derive chronic ReV and ESL values.

4.1.1 Physical/Chemical Properties

Physical/chemical properties for n-BA are discussed in Section 3.1.1.

4.1.2. Key Study

4.1.2.1 Bernard et al. (1996)

In a subchronic neurotoxicity inhalation study by Bernard et al. (1996), as cited in DECOS (2001), male and female SD rats (n=30-40/group) were exposed to 0, 500, 1,500, 3,000 ppm (nominal concentrations) of n-BA vapor, 6 h/day, 5 day/week, for 13-14 weeks. Endpoints evaluated were functional observational battery (FOB) and motor activity (during weeks 1-13 in 10-15 animals/sex/group), neuropathology (gross and microscopic examination of tissue from the brain, spinal cord, dorsal and ventral spinal roots, dorsal root ganglia, sciatic nerve, and tibial nerve at study termination in 5 animals/sex/group), and scheduled-controlled operant behavior (SCOB) during exposure and two weeks post-exposure in 10 feed-restricted male animals/group. No treatment-related effects indicative of neurotoxicity were observed in the FOB, motor activity, SCOB, or gross and microscopic examinations of nervous system tissues in any of the exposure groups.

In the *ad libitum*-fed animals of the 3,000 ppm exposed groups, treatment caused lower mean body weights throughout the study resulting in an overall decrease of 15-19% and lower mean body weight gains for males throughout the study and for females during the first six weeks resulting in an overall decrease of 36-41%. Exposure to 3,000 ppm further induced signs of sialorrhea, gasping, and red discoloration of the chin, as well as reduced activity levels (hypoactivity defined as less movement, decreased alertness, and slower response to tapping on the chamber wall in comparison with control animals) of "minor" severity. In the 1,500 ppm exposed group, no effects were observed on body weights of the male animals; while those of

females were lowered from week 6 onwards (overall decrease 9%). Mean body weight gain was affected occasionally (male, week 9, 14; female, week 6, 11) with an overall decrease of 16-26%. In addition, reduced activity of "minimal" severity was observed. No such effects were observed in the group exposed to 500 ppm.

The study demonstrated that exposure to up to 3,000 ppm n-BA for 13 weeks did not induce persistent neurotoxic effects in rats. However, exposure to 1,500 ppm caused minimal to mild necrosis of the olfactory epithelium, decreased body weight gain, and decreased transient motor activity (nervous system). A subchronic LOAEL of 1,500 ppm ($\approx 7,100$ mg/m^3) and NOAEL of 500 ppm ($\approx 2,380$ mg/m^3) for minimal to mild necrosis of the olfactory epithelium, transient sedation or hypoactivity, and reductions in body weight gain were identified from this study. Since no data on effects following chronic exposure were available, the subchronic NOAEL of 500 ppm which was the highest reported NOAEL was used as the POD for deriving the chronic ReV and ESL.

4.1.3 Supporting Studies

4.1.3.1 David et al. (1998)

In a subchronic neurotoxicity inhalation study conducted by David et al. (1998), groups of 30–40 SD rats in each sex were exposed to n-BA vapor at 0, 500, 1,500, or 3,000 ppm ($\pm 10\%$), 6 h/day, 5 days/week, for 65 exposures over 14 weeks. FOB and motor activity values, and SCOB were measured during weeks 1, 4, 8, and 13; and at the end of the exposure period. Five *ad libitum*-fed animals per sex were randomly selected from each exposure group for neurohistopathology examination. Clinical observations were made through the inhalation chamber windows before, during, and after exposure and during the FOB test. Transient signs of sedation and hypoactivity were observed only during exposure to the 1,500 ppm and 3,000 ppm exposure groups. Reduced body weights were observed in the 3,000 ppm *ad libitum-fed* groups and occasionally in the female 1,500 ppm *ad libitum*-fed group. No treatment-related effects indicative of neurotoxicity were observed in the FOB, motor activity, SCOB, or gross and microscopic examinations in any of the exposure groups.

The authors concluded that exposures to n-BA vapor resulted in acute, transient signs of reduced activity levels on a daily basis at 1,500 ppm ($\approx 7,100$ mg/m^3) and 3,000 ppm ($\approx 14,200$ mg/m^3), but there was no evidence of cumulative neurotoxicity based on the FOB, motor activity measurement, microscopic examination of nervous system tissues, and SCOB endpoints. The results of this study were consistent with those observed by Bernard et al. (1996). A NOAEL of 500 ppm ($\approx 2,380$ mg/m^3) for reductions in activity levels and body weight gain was identified from this study.

4.1.3.2 David et al. (2001)

The subchronic toxicity of n-BA was evaluated in rats in conjunction with the neurotoxicity study by David et al. (1998, 2001). Groups of 15 male and 15 female SD rats were exposed to target vapor concentrations of approximately 0, 500, 1,500, or 3,000 ppm ($\pm$ 10%), 6 h/day, 5 days/week for 13 weeks. On day 30, five animals per sex per group were killed for clinical pathology. There was no compound-related mortality in any of the groups. In the 3,000 ppm group, all animals showed slightly reduced activity. Mean body weights and food intake were generally lower than those of the control animals throughout the study.

At the end of the study, body weights and feed consumption, clinical observations and histopathology were examined. The results showed that acute, transient signs of reduced activity levels were observed during exposure to 1,500 and 3,000 ppm. Decreased body weight and feed consumption were noted for the 1,500 and 3,000 ppm groups, but there was no systemic or organ-specific toxicity. Degeneration of the olfactory epithelium at the concentrations of 1,500 and 3,000 ppm was observed in areas of the nasal cavity, but there was no evidence of pulmonary toxicity. The severity of the olfactory lesion was minimal to mild for the 1,500 ppm group and mild to moderate for the 3,000 ppm group. No treatment-related effects were observed in the 500 ppm exposure group. A NOAEL of 500 ppm ($\approx$ 2,380 mg/m^3) was identified from this study.

4.1.4 MOA Analysis and Dose Metric

As described in Section 3.1.6, n-BA is quickly hydrolyzed to acetic acid and n-butanol in the blood, liver, small intestine, and respiratory tract. n-BA is probably excreted via exhaled air and urine both as the unchanged compound and as metabolites (butanol, butyraldehyde, and butyrate) after transformation in the body (IPCS 2005). Degeneration of the olfactory epithelium in the nasal cavity was observed in areas that have demonstrated high levels of carboxylesterases which metabolize acetates to their corresponding acid and alcohol, which causes the olfactory epithelium to be sensitive to acetates. The lesions in the olfactory epithelium of animals exposed to n-BA are probably the results of hydrolysis of the ester leading to the following of n-butanol and acetic acid (Bogdanffy 1990, as cited in David et al. 2001). Humans exposed to atmospheres containing n-BA at a concentration of 200 mg/m^3 were reported to excrete 50% of the inhaled compound in the exhaled air (DECOS 2001). Many chronic systemic effects (e.g., neurotoxicity) of n-BA are transient, of low adversity/severity, or apparently nonspecific, such as decreases in body weight gain (Bernard et al. 1996, David et al. 1998, Barton et al. 2000). These effects appear to be concentration dependent and are assumed to have a threshold or nonlinear dose-response relationship.

Data on the exposure concentration of the parent chemical are available, whereas data on more specific dose metrics are not available. Exposure concentration of the parent chemical will be used as the default dose metric.

4.1.5 POD for the Key Study and Critical Effect

The subchronic NOAEL of 500 ppm for transient sedation, reductions in body weight gain, olfactory lesions, and decreased transient motor activity (nervous system) identified from the Bernard et al. (1996) study was used as the POD for deriving the chronic ReV. The reported NOAELs of 500 ppm from the supporting studies (David et al. 1998, 2001) were the same as the NOAEL from the key study. The critical effects noted in rats are considered relevant to humans although, humans may be less susceptible to the degeneration of olfactory epithelium (OECD 2001) because rats are obligate nose-breathers and the delivered dose to the olfactory epithelium is higher in rats than humans

4.1.6 Dosimetric Adjustments

4.1.6.1 Exposure Duration Adjustments

According to the TCEQ Guidelines (TCEQ 2012), the subchronic POD of 500 ppm was then adjusted from discontinuous exposure (6 h/d for 5d/wk) to continuous exposure concentration using the following dosimetric adjustments:

$$POD_{ADJ} = POD \times D/24 \times F/7$$
$$POD_{ADJ} = 500 \text{ ppm} \times 6/24 \times 5/7$$
$$POD_{ADJ} = 89.28 \text{ ppm}$$

where:

POD_{ADJ} = POD from an animal study, adjusted to a continuous exposure duration

POD = POD from an animal study, based on a discontinuous exposure duration

D = exposure duration, hours per day

F = exposure frequency, days per week

4.1.6.2 Default Dosimetry Adjustments from Animal-to-Human Exposure

4.1.6.2.1 Adjustments of n-BA as a Category 3 Vapor

Subchronic exposures to n-BA cause decreased growth, decreased transient motor activity (nervous system) which are systemic rather than point-of-entry (POE) respiratory effects. In addition, the physical/chemical parameters of n-BA indicate the potential for n-BA to be absorbed via the lungs and widely distributed within the body (Section 4.1.1). n-BA was therefore considered a Category 3 vapor (USEPA 1994). For Category 3 vapors, the default dosimetric adjustment from an animal concentration to a human equivalent concentration (POD_{HEC}) is conducted using the following equation:

$$POD_{HEC} = POD_{ADJ} \times [(H_{b/g})_A / (H_{b/g})_H]$$

The measured blood/air partition coefficients in the rat $((H_{b/g})_A)$ and human $((H_{b/g})_H)$ for n-BA are 1,160 and 677, respectively (Kaneko et al. 1994, as cited in IPCS 2005). Because the ratio of the animal-to-human partition coefficients (1,160/677 = 1.7) is greater than one, a default value of one is used as the regional gas dose ratio (RGDR) (i.e., $(H_{b/g})_A/(H_{b/g})_H$) (TCEQ 2012). The resulting POD_{HEC} from the POD of 89.28 ppm in the Bernard et al. (1996) study is 89.28 ppm.

4.1.6.2.2 Adjustments of n-BA as a Category 1 Vapor

Subchronic exposures to n-BA also caused minimal to mild necrosis of the olfactory epithelium, which is contact site toxicity or a POE effect in the extrathoracic region. Default dosimetric adjustments from animal-to-human exposure for n-BA was conducted as a Category 1 vapor based on updated animal-to-human dosimetric recommendations in USEPA (2012). The default regional gas dose ratio for the extrathoracic region ($RGDR_{ET}$) is 1. For Category 1 gases, the default dosimetric adjustment from animal-to-human exposure is conducted using the following equation:

$$POD_{HEC} = POD_{ADJ} \times RGDR_{ET}$$
$$= 89.28 \text{ ppm} \times 1$$
$$= 89.28 \text{ ppm}$$

4.1.7 Adjustments of the POD_{HEC}

The POD_{HEC} of 89.28 ppm (for necrosis of the olfactory epithelium) obtained from the default dosimetric adjustment for Category 1 gases was the same as the POD_{HEC} of 89.28 ppm (for decreased growth, decreased transient motor activity) obtained from the default dosimetric adjustment for Category 3 gases. Thus the POD_{HEC} of 89.28 was used to set the chronic ReV and $^{chronic}ESL_{threshold(nc)}$. The following UFs were applied to the POD_{HEC}:

- a UF_H of 10 for intraspecies variability. The TCEQ believes that a UF_H of 10 is sufficient to account for human variation including possible child/adult differences. There is no data that indicate that a UF_H larger than 10 is needed to protect children or other sensitive sub groups
- a UF_A of 3 for interspecies variability because a default dosimetric adjustment was conducted to account for toxicokinetic differences between animals and humans but not toxicodynamic differences,
- a UF_{Sub} of 1 instead of 10 for extrapolation from subchronic to chronic was used. The subchronic effects found in the key study are concentration dependent and metabolites of n-BA do not accumulate. Therefore, chronic effects would not be expected to differ significantly from subchronic effects (Barton et al. 2000, David et al. 2001, TCEQ 2012), and
- a UF_D of 3 was used because only one animal species was studied. Confidence in the database is considered medium to low because only one animal species was used in inhalation bioassays. The total UF = 90.

$$\text{Chronic ReV} = \text{POD}_{HEC} / (\text{UF}_H \text{ x } \text{UF}_A \text{ x } \text{UF}_{Sub} \text{ x } \text{UF}_D)$$
$$= 89.28 \text{ ppm} / (10 \text{ x } 3 \text{ x } 1 \text{ x } 3)$$
$$= 0.9914 \text{ ppm}$$
$$= 990 \text{ ppb (rounded to two significant figures)}$$

4.1.8 Health-Based Chronic ReV and ^{chronic}ESL$_{threshold(nc)}$

Accordingly, by applying a total UF of 100 to the POD$_{HEC}$ of 89.28 ppm, the chronic ReV is 990 ppb (4,700 µg/m^3). The ^{chronic}ESL$_{threshold(nc)}$ of 300 ppb (1,400 µg/m^3) was based on the chronic ReV multiplied by a HQ of 0.3 according to the TCEQ Guidelines (2012) as shown in Table 6.

Table 6 Derivation of the Chronic ReV and ^{chronic}ESL$_{threshold(nc)}$

Parameter	Summary
Study	Bernard et al. 1996
Study Population	Male and female SD rats
Study Quality	High
Exposure Method	Inhalation exposure of rats to 0, 500, 1,500, 3,000 ppm n-BA vapor
Critical Effects	Minimal to mild necrosis on the olfactory epithelium, decreased transient motor activity (CNS effects), and decreased growth
LOAEL	1,500 ppm
POD (NOAEL)	500 ppm
Exposure Duration	6 h/day, 5 day/week, for 13 weeks
Extrapolation to continuous exposure (POD$_{ADJ}$)	89.28 ppm
POD$_{HEC}$	89.28 ppm
Total UFs	90
Interspecies UF	3
Intraspecies UF	10
LOAEL-to-NOAEL UF	Not applicable
Subchronic to chronic UF	1
Incomplete Database UF	3
Data Quality	Medium to low
Chronic ReV (HQ = 1)	**4,700 µg/m^3 (990 ppb)**

Parameter	Summary
chronicESL$_{threshold(nc)}$ (HQ = 0.3)	1,400 μg/m^3 (300 ppb)

4.2 Carcinogenic Potential

n-BA has been tested adequately at sufficiently high concentrations in bacteria (*Salmonella typhimurium,* Escherichia coli), yeast (Saccharomyces cerevisiae) and one mammalian cell system (Chinese hamster lung fibroblasts). The results indicate a lack of genotoxic potential. n-BA was not mutagenic to Salmonella typhimurium (Ames test) and failed to induce chromosomal damage or effects in human lymphocytes or Chinese hamster cells in vitro (IPCS 2005). No data were found on long-term toxicity or carcinogenicity studies on n-BA. No adequate data were identified from studies in laboratory animals on which direct conclusions regarding carcinogenicity can be based. Because there is no available data to assess carcinogenicity in humans via the inhalation route, the $^{chronic}ESL_{nonthreshold(c)}$ was not developed.

4.3 Welfare-Based Chronic ESL

No information was found to indicate that special consideration should be given to possible chronic vegetation effects from n-BA.

4.4 Long-Term ESL and Values for Air Monitoring Evaluation

This chronic evaluation resulted in the derivation of the following chronic values:

- chronic ReV = 4,700 $\mu g/m^3$ (990 ppb)
- $^{chronic}ESL_{threshold(nc)}$ = 1,400 $\mu g/m^3$ (300 ppb)

For the evaluation of ambient air monitoring data, the chronic ReV of 4,700 $\mu g/m^3$ (990 ppb) is used (Table 1). The long-term ESL for air permit evaluations is the $^{chronic}ESL_{threshold(nc)}$ of 1,400 $\mu g/m^3$ (300 ppb) (Table 2). The $^{chronic}ESL_{threshold(nc)}$ (HQ = 0.3) is not used for evaluation of air monitoring data.

4.5 Chronic Observed Adverse Effect Level

The LOAEL value of 1,500 ppm determined in a rat 13-wk study (Bernard et al. 1996) (Table 6) was used as the POD for calculation of a chronic inhalation observed adverse effect level. No duration adjustment was made (TCEQ 2012). However, an animal-to-human dosimetric adjustment was made to calculate a $LOAEL_{HEC}$:

The $LOAEL_{HEC}$ was calculated using the following equation:

$$LOAEL_{HEC} = LOAEL \times RGDR_{ET} \text{ (Section 4.1.6.2)}$$
$$= 1,500 \text{ ppm } \times 1$$
$$= 1,500 \text{ ppm}$$

The $LOAEL_{HEC}$ determined from an animal study, where effects occurred in some animals, represents a concentration at which it is possible that similar effects could occur in some individuals exposed to this level over the same duration as used in the study or longer.

Importantly, effects are not a certainty due to potential interspecies and intraspecies differences in sensitivity. The chronic inhalation observed adverse effect level of 7,100 mg/m^3 (1,500 ppm) is provided for informational purposes only (TCEQ 2012). As the basis for development of inhalation observed adverse effect levels is limited to available data, future studies could possibly identify a lower POD for this purpose.

The margin of exposure between the chronic inhalation observed adverse effect level of 1,500 ppm to the chronic ReV of 0.990 ppm is a factor of approximately 1,500.

Chapter 5 References

5.1. References Cited in DSD

American Conference of Governmental Industrial Hygienists (ACGIH). 2001. Documentation of the Threshold Limit Values for n-Butyl Acetate, Cincinnati, OH.

Barton HA, PJ Deisinger, JC English et al. 2000. Family approach for estimating reference concentrations/doses for series of related organic chemicals. *Toxicol Sci* 54: 251–261.

Bernard LG, RM David, RS Hosenfeld. 1996. n-Butyl acetate. A thirteen-week subchronic inhalation neurotoxicity study in the rat. As referenced in IPCS (2005).

Bowen SE and RL Balster. 1997. A comparison of the acute behavioral effects of inhaled amyl, ethyl, and butyl acetate in mice. *Fundam Appl Toxicol* 35: 189-196.

ChemIDplus Advanced, Physical Properties for n-Butyl Acetate (RN: 123-86-4), U.S. National Library of Medicine. Available from: http://chem.sis.nlm.nih.gov/chemidplus/ProxyServlet?objectHandle=DBMaint&actionHandle=default&nextPage=jsp/chemidlite/ResultScreen.jsp&TXTSUPERLISTID=000123864

Cosmetic Ingredient Review Expert Panel (CIREP). 1989. Final Report on the Safety Assessment of Ethyl Acetate and Butyl Acetate. *J Am Coll Toxicol* 8(4): 681-705.

David RM, TR Tyler, R Ouellette, et al. 1998. Evaluation of subchronic neurotoxicity of n-butyl acetate vapor. *Neurotoxicology* 19: 809-22.

David RM, TR Tyler, R Ouellette, et al. 2001. Evaluation of subchronic toxicity of *n*-butyl acetate vapor. *Food Chemical Toxicol* 39:877–886.

Dravnieks, A. 1974. A building-block model for the characterization of odorant molecules and their odors. *Ann N Y Acad Sci* 237 (0):144-63.

Dutch Expert Committee on Occupational Standards (DECOS). 2001. n-, iso-, sec-, and tert-Butyl acetate: Health-based recommended occupational exposure limit. Health Council of the Netherlands. Pub No. 2001/03OSH, The Hague, Netherlands. Available from: http://www.gezondheidsraad.nl/sites/default/files/01@03OSH.PDF

Hellman TM and FH Small. 1973. Characterization of petroleum chemical odors. *Chem Eng Progr* 69: 75-77.

Hellman TM and FH Small. 1974. Characterization for the odor properties of 101 petrochemicals using   sensory methods. *J Air Pollut Control Assoc* 24: 979-982.

International Programme on Chemical Safety (IPCS). 2005. Concise International Chemical Assessment Document 64: Butyl Acetates. World Health Organization. Geneva, Switzerland. Available from: http://www.inchem.org/documents/cicads/cicads/cicad64.htm

Iregren A, A Lof, A Toomingas et al. 1993. Irritation effects from experimental exposure to n-butyl acetate. *Am J Ind Med* 24: 727-742.

May, J. 1966. Geruchsschwellen von Losemitteln zur Bewetertug von Losemittelgeruchen in der Luft [Odor thresholds of solvents for assessment of solvent odors in the air] *Staub Reinhalt* 26 385-389.

Nagata Y. 2003. Measurement of odor threshold by triangle odor bag method. Odor Measurement Review, Japan Ministry of the Environment. Pp. 118-127. Available from: http://www.epa.gov/oppt/aegl/pubs/rest101.htm

National Institute for Occupational Safety and Health (NIOSH)/Occupational Safety and Health Administration. 1978. Occupational Health Guideline for Butyl Acetate. Center for Disease Control and Prevention, U.S. Health and Human Services, NIOSH Pub No. 81-123. Cincinnati, OH.

Nelson KW, JF Ege, M Ross, et al. 1943. Sensory response to certain industrial solvent vapors. *J Ind Hyg Toxicol* 25: 282-285.

Norris JC, DJ Nachreiner, TR Tyler, et al. 1997. Acute inhalation toxicity studies of n-butyl acetate. *Inhalation Toxicol* 9: 623-646.

Organization for Economic Co-Operation and Development (OECD). 2009. Screening Information Data Set (SIDS) Initial Assessment Report for n-Butyl Acetate. Chemicals SIDS for High Volume Chemicals. Available from: http://www.oecd.org/document/63/0,3343,en_2649_34379_1897983_1_1_1_1,00.html

TCEQ. 2012. TCEQ guidelines to develop toxicity factors (Revised RG-442). Texas Commission on Environmental Quality. Office of the Executive Director. Available from: http://www.tceq.texas.gov/publications/rg/rg-442.html

Texas Commission on Environmental Quality (TCEQ). (2015). Approaches to derive odor-based values. Texas Commission on Environmental Quality. Office of the Executive Director, Austin, TX.

United States Environmental Protection Agency (USEPA). 1994. Methods for derivation of inhalation reference concentrations and application of inhalation dosimetry. EPA/600/8-90/066F. Office of Research and Development. Washington, DC.

United States Environmental Protection Agency (USEPA). 2012 Advances in inhalation gas dosimetry for derivation of a reference concentration (RfC) and use in risk assessment. Washington, D.C. EPA/600/R-12/044).

van Doorn R, MW Ruijten, and T van Harreveld. 2001. Guidance for the Application of Odor in the Derivation of AEGL-1. Version 02/06/2001. Presented at the NAC/AEGL-Meeting.

van Doorn R, MW Ruijten, and T van Harreveld. 2002. Guidance for the Application of Odor in Chemical Emergency Response. Version 2.1; August 29, 2002. Presented at the NAC/AEGL-Meeting September 2002, Washington DC.

van Harreveld, AP. 2003. Odor Regulation and the History of Odor Measurement in Europe. Odor Review, Japan Ministry of the Environment. Pp. 54-61. Available from: http://www.env.go.jp/en/air/odor/measure/02_1_3.pdf