n-Butanol (CAS#71-36-3) GreenScreen® for Safer Chemicals (GreenScreen®) Assessment

Prepared by:

ToxServices LLC

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TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING
1367 Connecticut Ave., N.W., Suite 300
Washington, D.C. 20036

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GreenScreen® Executive Summary for n-Butanol (CAS #71-36-3)

n-Butanol is a clear, colorless liquid that is flammable. It is classified as a primary alcohol and is used primarily as a chemical intermediate, as an ingredient in formulated products such as cosmetics, and as a solvent.

n-Butanol was assigned a GreenScreen® Benchmark Score of 2 ("Use but Search for Safer Substitutes") as it has a Very High Group II Human Toxicity (Very High eye irritation, IrE). This corresponds to GreenScreen® benchmark classification 2f in CPA 2011. Data gaps (DG) exist for endocrine activity (E) and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), n-butanol meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gap. In a worst-case scenario, if n-butanol were assigned a High score for data gap endocrine Activity (E) it would be categorized as a Benchmark 1 Chemical.

GreenScreen® Benchmark Score for Relevant Route of Exposure:
As a standard approach for GreenScreen® evaluations, all exposure routes (oral, dermal and inhalation) were evaluated together, so the GreenScreen® Benchmark Score of 2 ("Use but Search for Safer Substitutes") is applicable for all routes of exposure.

GreenScreen® Hazard Ratings for n-Butanol

Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
C	M	R	D	E	AT	ST		N		SnS*	SnR*	IrS	IrE	AA	CA	P	B	Rx	F
						single	repeated*	single	repeated*										
L	**L**	**L**	**L**	DG	**M**	**M**	**L**	DG	**L**	*L*	DG	**H**	**vH**	**L**	**L**	**vL**	*vL*	*L*	**H**

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated values, authoritative B lists, screening lists, weak analogues, and lower confidence. Hazard levels in **BOLD** font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M, and L) instead of three (i.e., H, M, and L), and are based on single exposures instead of repeated exposures. Please see Appendix A for a glossary of hazard acronyms.

GreenScreen® Assessment for n-Butanol (CAS # 71-36-3)

GreenScreen® Version 1.2 Draft Assessment
Note: Verification Has Not Been Performed on this GreenScreen® Assessment

Chemical Name: n-Butanol

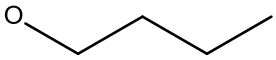
CAS Number: 71-36-3

GreenScreen® Assessment Prepared By:
Name: Mouna Zachary, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: March 17, 2014

Quality Control Performed By:
Name: Dr. Margaret H. Whittaker, Ph.D., M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Title: Managing Director and Chief Toxicologist
Organization: ToxServices LLC
Date: June 25, 2014

Confirm application of the *de minimus* rule[1]: Not applicable for n-butanol; not a mixture.

Chemical Structure(s):

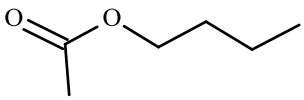


n-Butanol (CAS#71-36-3)

Also called: 1-Butanol; Butyl alcohol; n-Butyl alcohol; Butyl alcohol; Propyl carbinol; Butanol, 1-; n-Butan-1-ol; 1-Hydroxybutane; Butyl hydroxide; Propylmethanol; Butanolen; Butyric alcohol; Methylolpropane (ChemIDplus 2014)

Chemical Structure(s) of Chemical Surrogates Used in the GreenScreen®:

For some endpoints, insufficient reliable data are available for n-butanol. Therefore, n-butyl acetate (CAS #123-86-4) is used as a surrogate. This surrogate has been used to support the safety of n-butanol by OECD (UNEP 2001). A GLP-compliant *in vivo* toxicokinetic study in rats using radiolabeled butyl acetate demonstrated that 99% of the intravenously administered butyl acetate was hydrolyzed in the blood and brain within 2.7 minutes to form n-butanol (TSL 1997). Therefore, toxicity studies on butyl acetate provide information on the toxicity of butanol for endpoints relevant to the systemic blood levels. It should be noted that data on butyl acetate may not be relevant for n-butanol for site-of-contact effects and other physical-chemical property-dependent endpoints (UNEP 2001).



n-Butyl acetate (CAS #123-86-4)

[1] Every chemical in a material or formulation should be assessed if it is:
1. intentionally added and/or
2. present at greater than or equal to 100 ppm

Identify Applications/Functional Uses:

1. Solvent for paints, lacquers, varnishes, resins, gums, vegetable oils, dyes and alkaloids (HSDB 2010).
2. An intermediate in the manufacture of pharmaceuticals and chemicals (HSDB 2010).
3. Employed in industries producing artificial leather, textiles, safety glass, rubber cement, shellac, raincoats, photographic films and perfumes (HSDB 2010).
4. Additives in beverages and foods (HSDB 2010).

GreenScreen® Summary Rating for n-Butanol[2]: n-Butanol was assigned a GreenScreen® Benchmark Score of 2 ("Use but Search for Safer Substitutes") as it has Very High Group II Human Toxicity (eye irritation, IrE). This corresponds to GreenScreen® benchmark classification 2f in CPA 2011. A data gap (DG) exist for endocrine activity (E) and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), n-butanol meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gap. In a worst-case scenario, if n-butanol were assigned a High score for data gap endocrine activity (E) it would be categorized as a Benchmark 1 Chemical.

Figure 1: GreenScreen® Hazard Ratings for n-Butanol

Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
C	M	R	D	E	AT	ST		N		SnS*	SnR*	IrS	IrE	AA	CA	P	B	Rx	F
						single	repeated*	single	repeated*										
L	L	L	L	DG	M	M	L	DG	L	*L*	DG	H	vH	L	L	vL	*vL*	*L*	H

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated (modeled) values, authoritative B lists, screening lists, weak analogues and lower confidence. Hazard levels in **BOLD** font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e. vH, H, M, and L) instead of three (i.e. H, M, and L), and are based on single exposures instead of repeated exposures. Please see Appendix A for a glossary of hazard acronyms.

Transformation Products and Ratings:

Identify feasible and relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern**[3]

No environmental transformation products were identified from the literature for n-butanol. n-Butanol is considered a volatile organic compound (VOC) and is readily degradable in water and readily decomposed in the air by photodegradation. It does adsorb on soil, and favors partitioning to water versus air (80% to 15-20%). Based on its molecular formula, possible combustion products of n-butanol are CO and CO_2, which are naturally occurring, ambient substances and not relevant with respect to the GreenScreen® Benchmark score for n-butanol.

[2] For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.

[3] A moiety is a discrete chemical entity that is a constituent part or component of a substance. A moiety of concern is often the parent substance itself for organic compounds. For inorganic compounds, the moiety of concern is typically a dissociated component of the substance or a transformation product.

Introduction

n-Butanol is a clear, colorless liquid that is flammable. It has a characteristic banana-like odor and is used to produce other chemicals, as an ingredient in formulated products such as cosmetics, and as a solvent (HSDB 2010). Over 10 billion pounds of n-butanol was consumed world-wide in 2002 (Dow 2014). ToxServices assessed n-butanol against GreenScreen® Version 1.2 (CPA 2013) following procedures outlined in ToxServices' SOP 1.37 (GreenScreen® Hazard Assessment) (ToxServices 2013).

GreenScreen® List Translator Screening Results

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen® benchmark 1 chemicals (CPA 2012b). Pharos (Pharos 2014) is an online list-searching tool that is used to screen chemicals against the List Translator electronically. It checks all of the lists in the List Translator with the exception of the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b) and these should be checked separately in conjunction with running the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for n-butanol can be found in Appendix C, and classifications for specific endpoints can be found in the appropriate sections. When a classification from GHS New Zealand was available for any endpoint, it was converted to the harmonized GHS classifications using the "Correlation between GHS and New Zealand HSNO Hazard Classes and Categories" document from the New Zealand Environmental Protection Authority (N.Z. EPA 2009).

PhysicoChemical Properties of n-Butanol

The physicochemical properties of n-butanol are summarized in Table 1. n-Butanol is a colorless liquid that is partially soluble in water and volatile at room temperature. Its partition coefficient of 0.88 indicates that it is highly hydrophilic.

Table 1: Physical and Chemical Properties of n-Butanol (CAS # 71-36-3)

Property	Value	Reference
Molecular formula	$C_4H_{10}O$	ChemIDplus 2014
SMILES Notation	C(CC)CO	ChemIDplus 2014
Molecular weight	74.122	ChemIDplus 2014
Physical state	Liquid	ChemIDplus 2014
Appearance	Colorless liquid	HSDB 2010
Melting point	-89.8°C	ChemIDplus 2014
Vapor pressure	6.7 mmHg at 25ºC	ChemIDplus 2014
Water solubility	63.2 g/L at 25ºC	ChemIDplus 2014
Dissociation constant	16.1 at 25ºC	ChemIDplus 2014
Density/specific gravity	0.8098 at 20ºC/4ºC	HSDB 2010
Partition coefficient	0.88	ChemIDplus 2014

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M, or L): *L*

n-Butanol was assigned a score of Low for carcinogenicity based on weight of evidence. GreenScreen® criteria classify a chemical as a Low hazard for carcinogenicity when adequate and negative data are available, there are no structural alerts, and they are not GHS-classified (CPA 2012a).

Authoritative and Screening Lists

- *Authoritative:* U.S. EPA – IRIS Carcinogen (EPA-C): (1986) Group D – Not classifiable as to human carcinogenicity
- *Screening:* Not listed on any screening lists.

- UNEP 2001 –
  - There were no reliable data on n-butanol regarding carcinogenicity. However, based on n-butanol's negative mutagenicity and clastogenicity, it presents a very small potential for carcinogenicity.

Mutagenicity/Genotoxicity (M) Score (H, M, or L): L

n-Butanol was assigned a score of Low for mutagenicity/genotoxicity based on negative results obtained from *in vitro* and *in vivo* mutagenicity/genotoxicity assays. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when adequate data are available and negative and they are not classified under GHS (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists
  - *Screening:* Not listed on any screening lists.
- ECETOC 2003
  - n-Butanol tested negative in a number of Ames tests using *S. typhimurium* strains TA98, TA100, TA102, UTH8413, UTH8414, TA1535 and TA1537 in the presence and absence of metabolic activation at concentrations of up to 5,000 µg/late.
  - n-Butanol induced aneuploidy during early germination of *Aspergillus nidulans* at concentrations of up to 1%.
  - n-Butanol tested negative for chromosome aberrations in Chinese hamster lung fibroblast cells and sister chromatid exchange in Chinese hamster ovary cells at concentrations of 810 – 40,500 µg/mL in absence of metabolic activation.
  - In an *umu* test using *S. typhimurium* strain TA1535/pSK1002, concentrations of up to 27,000 µg/mL did not increase DNA repair in the presence and absence of metabolic activation.
  - In an *in vivo* micronucleus assay, single oral dose of 0, 500, 1,000 or 2,000 mg/kg n-butanol did not increase the number of normochromatic and polychromatic erythrocytes containing either small or large micronuclei, inhibit erythropoiesis or induce aneuploidy in the bone marrow of male and female NMRI mice.
  - In an *in vivo* cytogenetic assay, up to 1,214 µg n-Butanol did not induce sister chromatid exchanges or chromosomal aberrations after 3 – 4 days in the Cornell K-strain chicken embryo.
- The weight of evidence for all genotoxicity toxicity testing indicates that n-butanol does not have a genotoxic potential (ECETOC 2003). Although n-butanol was positive in inducing aneuploidy in *Aspergillus nidulans*, it did not induce chromosome aberrations in mammalian cells *in vitro* and *in vivo*.

Reproductive Toxicity (R) Score (H, M, or L): L

n-Butanol was assigned a score of Low for reproductive toxicity based on no reproductive effects being observed in animal studies. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate data are available and are negative for reproductive toxicity, and the chemical is not present on authoritative or screening lists (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists.
- Inhalation
  - UNEP 2001
    - No detectable effect on pregnancy rate was found in female Sprague-Dawley rats (15/group) exposed throughout gestation or males (18) exposed for six weeks prior to mating with unexposed females at inhalation doses of 3,000 or 6,000 ppm n-butanol.
    - No changes in reproductive performance were observed in female rats exposed to 1,500 ppm of n-butanol for three weeks prior to mating and during gestation. The males were unexposed, however.
    - There was no evidence of testicular toxicity in male rats exposed via inhalation to 0, 500, 1,500, or 3,000 ppm of n-butanol (6 hrs/day) for at least 65 exposures over 14 weeks. Therefore, the NOAEL of 3,000 ppm for male reproductive toxicity following repeated inhalation exposure was established.
  - U.S EPA 2011
    - To study testicular toxicity, male Sprague-Dawley rats (5/group) received inhalation doses of 150 mg/m^3 n-butanol for 6 hours/day for 1 day or 1 week. Rats exposed for 1 day had statistically significant reductions in testosterone concentrations, but the decrease was not statistically significant in rats exposed for 1 week. Rats treated for 1 day had statistically significant increase in serum corticosterone, but those treated for 1 week had lower levels, which were not statistically significant. It is not clear if the temporary changes in hormone levels are of toxicological significance. Therefore, ToxServices did not assign an effect concentration for this study.
- Oral
  - UNEP 2001
    - No testicular toxicity was observed in male Sprague-Dawley rats given 533 mg/kg/day n-butanol in corn oil (via intubation) for six days even though an equimolar dose of its parent compound (2,000 mg/kg/day of dibutyl phthalate) did decrease testes weights, produce testicular atrophy, and alter zinc metabolism.
- The weight of evidence for the inhalation and oral studies in animals indicates that n-butanol is not a reproductive toxicant. Testicular toxicity was only seen in one inhalation study in rats of short duration where the changes were not clearly explained.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): L

n-Butanol was assigned a score of Low for developmental toxicity based on weight of evidence. GreenScreen®criteria classify as a Low hazard for developmental toxicity when adequate data are available and are negative for developmental toxicity, and when they are not classified under GHS (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* German MAK – List of Substances (MAK): Pregnancy Risk Group C
  - *Screening:* Not listed on any screening lists

- Oral
    - UNEP 2001, U.S EPA 2011
        - Female Wistar Imp:DAK rats (11-17/group) were exposed to n-butanol in drinking water at 0, 0.24, 0.8 or 4% (estimated by the authors to be 0, 300, 1,000 or 5,000 mg/kg/day) for 8 weeks prior to mating, for 3 weeks during mating period to untreated males, and through gestation periods. Treatment did not affect survival, food or water consumption, body weight, hemoglobin concentration, hematocrit or organ weights. There were no differences in estrous cycle duration or duration of individual states of the cycle. Pregnancy rate, number of corpora lutea or total implants, number of litters with resorptions, and number of pre- or post-implantation losses/litter were not affected. Mean fetal crown-rump length was statistically significantly reduced in the high dose group (5%). Statistically significant and dose-related increases in the litter incidences with any dilation (i.e., subarachnoid space and cerebral ventricles) or renal pelvis were found at all doses. The percentages of litters with internal hydrocephalus were statistically significantly increased at the mid and high doses, and the percentage of litters with external hydrocephalus was increased at the mid dose only. In addition, the percentages of litters with extra rib were statistically significantly higher at the high dose. The U.S. EPA assigned a 300 mg/kg/day LOAEL (the lowest dose tested), based on increased incidences of dilation of the subarachnoid space and of the lateral and/or third ventricle of the brain in the offspring.
        - Pregnant Sprague-Dawley rats (20/group) were given n-butanol in drinking water at daily doses of 316, 1,454, or 5,654 mg/kg/day on gestational days 0 – 20. Maternal body weight gain was significantly ($p<0.05$) decreased at the high dose. Food and water consumption were statistically significantly decreased at mid and high doses. Fetal body weight was statistically significantly decreased at the high dose. Statistically significant increase in skeletal variations (primarily short supernumerary ribs) and decreased degree of ossification were observed at the high dose, which were attributed to growth retardation by the authors. The incidence of litters with thymic remnant in the neck increased dose-dependently and the incidence at the high dose was twice that of the controls. The U.S. EPA identified 5,654 mg/kg/day as the LOAEL and 1,454 mg/kg/day as the NOAEL based on decreased fetal body weight and increased incidence of skeletal variations for developmental toxicity.
        - White rats (10-16/group) were administered n-butanol by gavage at approximately 1,300 mg/kg/day during gestational days 1 – 15, and sacrificed on gestational day 20. There were statistically significant increases in the percentage of pre- and post-implantation losses and in total fetal deaths. In addition, fertility index was reduced. ADH activity in fetal livers was reduced. Due to lack of study details, EPA did not identify an effect level for this study.
- Inhalation
    - UNEP 2001, U.S EPA 2011
        - Pregnant Sprague-Dawley rats (15-20/group) were exposed to n-butanol at inhalation doses of 0, 11, 18 or 24 mg/L for 7 hours/day on gestational days 1 – 19. Two dams died prior to sacrifice at the highest concentration. Food consumption was reduced in dams at the mid and high concentrations ($p<0.05$). There was a statistically significant concentration related decrease in fetus body weight at the mid and high concentrations. At the high dose, the percentages of fetuses with normal skeletal development were statistically significantly reduced, with rudimentary

cervical ribs as the primary skeletal malformation observed. The incidences of litters with skeletal malformations were statistically significantly increased at all concentrations and the incidence of litters with visceral malformations was statistically significantly increased at the highest concentration. The U.S. EPA identified the LOAEC at 11 mg/L/7h/day based on increased incidence of litters with skeletal variations.

- ECHA 2014
  - n-Butyl acetate,– A GLP-compliant 2-generation inhalation toxicity study was conducted according to OECD TG 416 and EPA OPPTS 870.3800. Sprague-Dawley rats (30/sex/group) were exposed to n-butyl acetate vapor (99.8% pure) via whole-body inhalation at 0, 750, 1,500 or 2,000 ppm 6 hours/day for at least 70 consecutive days prior to mating. F0 and F1 females were exposed continuously throughout mating and gestation through gestation day 20 (not exposed through gestation day 21 to lactation day 4). F0 and F1 maternal animals were exposed to n-butyl acetate via oral gavage at 0, 1,125, 2,250 or 3,000 mg/kg/day during lactation day 1-4, which was administered as 3 equal doses approximately 2 hours apart. Inhalation exposure for F0 and F1 females resumed on lactation day 5 and continued through the day prior to sacrifice. Inhalation exposure of F1 offspring was initiated on post natal dal (PND) 20. The age at mating was 17-weeks old for F0 animals and 15-16 weeks old for F1 animals. Parameters monitored included cage side observation, clinical observation, body weight, food consumption, estrous cyclicity, sperm parameters, litter observations (number and sex of pups, stillbirths, live births, postnatal mortality, presence of gross anomalies, body weights, and physical and behavioral abnormalities), gross necropsy, histopathology and organ weights. According to the ECHA record and the study authors, the LOAEC for local effects for F0 and F1 animals was identified as 750 ppm based on degeneration of the olfactory epithelium in the nasal cavity. The NOAEC and LOAEC for systemic toxicity for F0, F1 and F2 adult animals are 750 and 1,500 ppm, respectively, based on decreased body weight, body weight gains and/or food consumption. The NOAEC and LOAEC for developmental toxicity of F1 and F2 generations are 750 and 1,500 ppm, respectively, based on growth retardation (lower mean pup body weight and body weight gain, delays in attainment of post-weaning developmental landmarks) without effects on survival. The NOAEC for fertility for F0 and F1 animals is 2,000 ppm based on lack of adverse effects noted. 750, 1,500 and 2,000 ppm are equivalent to 2.26, 4.54 and 6.05 mg/L/6h/day n-butanol[4].

- The weight of evidence suggests that n-butanol causes developmental toxicity only at high doses which are significantly toxic to the dam. Therefore, n-butanol is not a selective developmental toxicant and a score of Low was assigned.

Endocrine Activity (E) Score (H, M, or L): DG

n-Butanol was assigned a score of data gap for endocrine disruption based on a lack of data for this endpoint.

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists.
- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.

[4] 750 ppm = (MW (n-butanol) x 750 ppm ÷ 24,450) mg/L = (74 x 750/24,450) mg/L = 2.26 mg/L

- Not listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.
- No data were identified.

Group II and II* Human Health Effects (Group II and II* Human)

Note: Group II and Group II* endpoints are distinguished in the v 1.2 Benchmark system. For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints and test data for single or repeated exposures may be used. If data exist for single OR repeated exposures, then the endpoint is not considered a data gap. If data are available for both single and repeated exposures, then the more conservative value is used.

Acute Mammalian Toxicity (AT) Group II Score (vH, H, M, or L): M

n-Butanol was assigned a score of Moderate for acute toxicity based on oral LD_{50} values being between 300-2,000 mg/kg and classification by authoritative lists. GreenScreen® criteria classify chemicals as a Moderate hazard for acute toxicity when oral LD_{50} values are between 300-2,000 mg/kg and when associated with EU R-phrase of R22 and H-Statement of H302 (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* EU R-Phrases: R22: Harmful if swallowed
  - *Authoritative:* EU H-Statements: H302: Harmful if swallowed
  - *Screening:* GHS-Japan: Acute toxicity (oral) – Category 4
  - *Screening:* GHS-Japan: Acute toxicity (dermal) – Category 5
  - *Screening:* GHS-New Zealand: Acutely toxic (oral) – 6.1D
  - *Screening:* GHS-New Zealand: Acutely toxic (dermal) – 6.1E
  - *Screening:* GHS-New Zealand: Acutely toxic (inhalation) – 6.1E
  - *Others::* Québec CSST – WHMIS: Class D2B – Toxic material causing other toxic effects
  - *Others:* GHS-Japan: Aspiration hazard– Category 2
- Oral -
  - UNEP 2001
    - LD_{50} of 790 – 4,360 mg/kg (rats)
    - LD_{50} of 2,680 mg/kg (mice)
    - LD_{50} of 3,500 mg/kg (rabbits)
    - LD_{50} of 1,200 mg/kg (hamsters)
    - LD_{50} of 1,782 mg/kg (dogs)
- Dermal -
  - UNEP 2001
    - LD_{50} of 3,402 – 7,500 mg/kg (rabbits)
- Inhalation -
  - UNEP 2001
    - LC_{50} of 8,000 ppm, equivalent to 24.2 mg/L[5] (4hr, rats)

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)

***Group II Score (single dose)* (vH, H, M, or L): M**

n-Butanol was assigned a score of Moderate for systemic toxicity (single dose) based on association with authoritative and screening lists. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (single dose) when they are associated with EU R-phrase of R37, EU-H-Statement of H335 and when they are classified to GHS category 3 (single exposure) by a screening list (CPA

[5] To convert concentrations in air (at 25°C) from ppm to mg/m^3: mg/m^3 = (ppm) × (molecular weight of the compound)/(24.45). For n-butanol: 1 ppm = 3.03 mg/m^3. Then to convert from mg/m^3 to mg/L: (mg/m^3) × 0.001

2012a)

- Authoritative and Screening Lists
  - *Authoritative:* EU R37: Irritating to respiratory system
  - *Authoritative:* EU H335: May cause respiratory irritation
  - *Screening:* GHS-Japan: Specific target organs/systemic toxicity following single exposure – Category 3
- UNEP 2001
  - The irritating effect of n-butanol on the respiratory system was studied in mice and it was predicted that 40 mg/m^3 (13 ppm) in air would have a minimal or no effect on humans, 390.9 mg/m^3 (127 ppm) would be uncomfortable, and 3,909 mg/m^3 (1,268 ppm) would be intolerable.

Group II* Score (repeated dose) **(H, M, or L): L**

n-Butanol was assigned a score of Low for systemic toxicity (repeated dose) based on animal studies on n-butanol and on surrogate; n-butyl acetate. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when animal studies identify oral LOAEL values greater than 100 mg/kg/day, dermal LOAEL values greater than 200 mg/kg/day and inhalation LOAEC values greater than 1.0 mg/L/6h/day for vapor (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative
  - *Screening:* GHS-Japan: Specific target organs/systemic toxicity following repeated exposure – Category 1
- Oral
  - U.S. EPA 2011
    - In a subchronic toxicity study, rats (30/sex/dose) received n-butanol via daily gavage at 0, 30, 125 or 500 mg/kg/day for 13 weeks. There were no treatment-related effects on body weight or organ weight changes, food consumption, mortality, gross pathology, histopathology and ophthalmic evaluations. At week 6, there were reduced hematocrit, erythrocyte count and hemoglobin content (5% lower) in high dose females, but no hematological changes were found in males or in either sex at terminal sacrifice. Sporadic changes in neutrophil count, lymphocyte count, cholesterol, urine pH and thyroid weight were found at one evaluation time only, and without a dose-response relationship. U.S. EPA assigned the NOAEL and LOAEL at 125 and 500 mg/kg/day, respectively based on reduced hematocrit, erythrocyte count and hemoglobin content in females.
    - In a subchronic toxicity study male Wistar rats (15/group) received n-butanol in drinking water at 0 or 8,200 mg/kg/day for 3 months. Toxicological evaluation was limited to electron microscopy of liver sections. Exposed animals had poor appetite, weakness and loss of body weight (no data were provided). Hepatic mitochondria were smaller with poorly developed cristae after 2 months of exposure. After 3 months, mitochondria were enlarged with little or no cristae, and some were cup-shaped or elongated. In addition, proliferation of smooth ER and increased numbers of lysosomes and microbodies were observed in the liver. U.S. EPA did not identify an effect level for this study due to limited parameters examined.
    - In another drinking water study focused on effects on protein synthesis in the brain, male Wistar rats (3/group) received n-butanol at 1% during the first week, 2% during the second week and 4% for up to 4 months, corresponding to a time-weighed concentration of 3.7% (4,400 mg/kg/day calculated by U.S. EPA). Only mortality,

body weight, selected serum chemistry parameters and *in vitro* protein synthesis of brain extract were examined. There were no mortalities, and body weight gain of treated animals was 46% of controls after 3 months. Signs of severe pathology were observed in several tissues, especially liver and kidney (no details) in treated animals, and they had statistically significantly higher total protein and albumin levels. U.S. EPA concluded that the information provided was inadequate to establish an effect level.

- Inhalation
  - U.S EPA 2011
    - In a subchronic toxicity study, male Wistar rats (12/exposure group, 24 controls) were exposed to n-butanol at vapor concentrations of 0, 50 or 100 ppm (0, 154 or 308 mg/m^3, calculated by the document) for 6 h/day, 5 days/week for 3 months. All rats survived to the end of the study without clinical abnormalities. There were no significant changes in mean body weight and absolute and relative organ weights. There was a statistically significant decrease in erythrocyte counts (16%) at the highest dose and in hemoglobin level (10%) in both exposure groups, but hematocrit was not changed. There were statistically significantly increased leukocyte counts and in the percentage of eosinophils at the highest dose. In addition, lipid peroxidation (16 and 30%) was statistically significantly increased in the liver in both exposure groups. Although decreased hemoglobin and increased lipid peroxidation were observed at 154 mg/m^3, the U.S. EPA considered the changes not biologically relevant. Therefore, ToxServices considered the NOAEC and LOAEC were 154 and 308 mg/m^3, based on decrease in erythrocyte counts, increased leukocyte counts and percentage of eosinophils, and increased lipid peroxidation in the liver.[6]
    - Guinea pigs (>3/group, sex and number not specified) were exposed to n-butanol vapor at 300 mg/m^3 every day for 2 weeks (duration not specified) and then 4h/day , 6 days/week for 1 – 2.5 months. Two control groups were also used, including one sham-treated and one untreated group. In animals treated for 64 exposures, decreased erythrocyte and lymphocyte counts were observed. Two of three animals in this group had hemorrhagic areas in the lungs and transient albuminuria. A second group tested at this concentration developed severe skin infections after 30th exposure and two died during the 38th exposure. These animals had decreased erythrocytes and hemoglobin and increased total leukocytes. The surviving animal gained weight with improved blood parameters at sacrifice. The authors indicated that all three animals in this group had toxic degeneration of the livers and kidneys. The third group was continued for 28 days, and similar changes in hematology were observed, along with central liver and marked renal degeneration. In the two control groups, one animal each died of skin infection. ToxServices assigned a 300 mg/m^3/day LOAEC based on hematological changes despite the limited available data.[7]
    - In a 4-month study, rats and mice were exposed to n-butanol at 0, 0.8, 6.6 or 40 mg/m^3 for 4 months (exposure duration and frequency not specified). Increased thyroid gland activity occurred in all groups. Pituitary-adrenal system was disrupted, eosinophilic response following administration of adrenocorticotropic

[6] 154 mg/m^3 x 1 m^3/1000 L = 0.154 mg/L
300 mg/m^3 x 1 m^3/1000 L = 0.300 mg/L
[7] 300 mg/m^3 x 1 m^3/1000 L = 0.3 mg/L

hormone was reduced, and oxygen demand was reduced in the "cold test" at 6.6 and 40 mg/m^3. The authors concluded that a NOAEC and LOAEC of 0.8 and 6.6 mg/m^3 could be established for this study.[8] However, the U.S. EPA considered information in this publication inadequate for the purpose of identifying effect levels.

- Dermal
  - ECETOC 2003
    - In a 21-day study, n-butanol was applied under occlusion to rabbit skin. Drying of the skin, cracking, furrowing and exfoliation of the epidermis were reported. No further details were reported. Reported data are insufficient to establish effect levels.
  - UNEP 2001
    - In another dermal study, application of 42 to 55 ml/kg n-butanol to the skin of rabbits, each day for 1 to 4 consecutive days, resulted in 100% mortality. However, 30 applications of 20 ml/kg (equivalent to 16,196 mg/kg[9]) over a period of six weeks did not produce any fatalities.
- Based on the above data, the inhalation LOAECs were between 0.2 – 1.0 mg/L/6h/day (the cut off for GHS category 2), while both the oral and dermal LOAELs were greater than the cut-off value for GHS category 2 (100 mg/kg for oral and 200 mg/kg for dermal). The available studies on inhalation exposure, which is a relevant route of concern for this chemical, however were performed decades ago and were non-GLP compliant. Therefore, data on the surrogate chemical n-butyl acetate are presented to support the safety of n-butanol.

Chemical Surrogate:

- TSL 1996a, TSL 1996b, ECHA 2014
  - n-Butyl acetate: - In a GLP-compliant two-week inhalation probe study in rats, Sprague-Dawley rats (10/sex/dose) were exposed to n-butyl acetate vapor (99.9% pure) at 0, 750, 1,500 or 3,000 ppm for 6 hours/day, 6 days/week. Half of the animals at each dose were given food *ad libidum* while the other half were feed-restricted. Clinical observation, feed consumption and body weight were monitored periodically. Neurological examinations were performed, which are discussed below under neurotoxicity endpoint. At study termination, lungs, liver and kidneys were weighted and gross pathology was performed. There was a statistically significant decrease in mean body weight in feed-restricted males at the 3,000 ppm dose on Day 14, compared to control rats. No other statistically significant, treatment related (non-neurological) changes were observed. Based on reduced body weight in males, ToxServices established the LOAEC and NOAEC at 3,000 and 1,500 ppm, respectively, which are equivalent to 7.78 and 3.89 and mg/L/6h/day n-butanol, respectively[10].
  - n-Butyl acetate: In a GLP-compliant subchronic inhalation toxicity study in rats, Sprague-Dawley rats (15/sex/dose) were exposed to n-butyl acetate vapor at 0, 500, 1,500 or 3,000 ppm for 6 hours/day, 5 days/week for 13 weeks. Acute but transient signs of reduced activity were observed at mid and high doses. Statistically significantly reduced body weight and feed consumption were also observed at these doses, but no systemic, organ-specific toxicity were found. Local signs of irritation were reported at

[8] 0.8 mg/m^3 x 1 m^3/1000 L = 0.0008 mg/L
40 mg/m^3 x 1 m^3/1000 L = 0.04 mg/L
[9] To convert ml/kg to mg/kg = (ml/kg) × (density of the compound (g/cm^3) × (1000). For n-butanol: density of the compound = 0.8098 g/cm^3.
[10] Based on the equation of ppm = (MW x ppm ÷ 24,450) mg/L, 1,500 ppm n-butyl acetate = 1500 ppm n-butanol = (1,500 x 74 ÷ 24,450) mg/L = 4.54 mg/L/6h n-butanol. As animals were dosed 6 days per week, the mean daily dose = 4.54 mg/L x 6/7 = 3.89 mg/L/6h/day.

upper respiratory region at mid and high doses. The authors established the NOEC and LOEC at 500 and 1,500 ppm for this study. These levels are equivalent to 1.08 and 3.24 mg/L/6h/day n-butanol, respectively[11].

- n-Butyl acetate: – In a GLP-compliant subchronic inhalation neurotoxicity study in rats, Sprague-Dawley rats (10/sex/dose) were exposed to n-butyl acetate vapor at 0, 500, 1,500 or 3,000 ppm for 6 hours/day, 5 days/week for 13 weeks. Animals at each concentration were separated into two groups, one group was fed food *ad libidum* and another group received restricted amount of food. No treatment related mortality was found. Mean body weight of animals at the high dose were 15-19% lower than that of control animals, and the body weight gain was 65% and 59% of males and females in control group. The mean body weight in the mid dose group was 9% lower than that of the control group. The body weight of the low dose group was comparable to controls. Based on decreased body weight, ToxServices established the NOAEC and LOAEC at 500 and 1,500 ppm, which are equivalent to 1.08 and 3.24 mg/L/6h/day n-butanol, respectively (see footnote in the study above).

- Studies identified on the surrogate n-butyl acetate were all conducted under GLP and are therefore more robust than the n-butanol studies. The lowest LOAEC/LOEC identified for n-butyl acetate was 500 ppm in 90-day studies, which is equivalent to 1.08 mg/L/6h/day n-butanol (see footnotes in studies described), which is above the GHS category 2 cut-off value of 1 mg/L/6h/day for vapor. Because adequate data on the surrogate n-butyl acetate were available, the GHS-Japan Specific target organs/systemic toxicity Category 1 classification was not used for hazard assignment.

Neurotoxicity (N)

***Group II Score (single dose)* (vH, H, M, or L):** DG

n-Butanol was assigned a score of data gap for neurotoxicity (single dose) based on a lack of data for this endpoint.

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists
- ECETOC 2003
  - No animal data were identified.

***Group II* Score (repeated dose)* (H, M, or L): L**

n-Butanol was assigned a score of Low for neurotoxicity (repeated dose) based on animal studies on surrogate; n-Butyl acetate. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (repeated dose) when adequate and negative data are available, there are no structural alerts, and they are not GHS-classified (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* EU H336: May cause drowsiness or dizziness
  - *Screening:* Not listed on any screening lists
- Oral
  - U.S. EPA 2011, RTI 1985
    - In a subchronic toxicity study, rats (30/sex/dose) received n-butanol via daily gavage at 0, 30, 125 or 500 mg/kg/day for 13 weeks. Clinical signs of toxicity, specifically hypoactivity and ataxia were reported at the high dose only. These signs occurred 2-

[11] Based on the equation of ppm = (MW x ppm ÷ 24,450) mg/L, 500 ppm n-butyl acetate = 500 ppm n-butanol = (500 x 74 ÷ 24,450) mg/L = 1.51 mg/L/6h n-butanol. As animals were dosed 6 days per week, the mean daily dose = 1.51 mg/L x 5/7 = 1.08 mg/L/6h/day.

3 minutes after dosing and lasted for less than 1 hour. They were first observed during week 8, infrequently through week 10, and reached highest incidences during weeks 11-13. U.S. EPA identified the LOAEL and NOAEL of 500 and 125 mg/kg/day, respectively, based on these neurotoxic signs.

- Inhalation
  - U.S. EPA 2011
    - In a 4-month study, rats and mice were exposed to n-butanol at 0, 0.8, 6.6 or 40 mg/m^3 for 4 months (exposure duration and frequency not specified). At 6.6 and 40 mg/m^3, narcosis induced by –n-butanol was shortened, and conditioned reflex activity increased. Other changes included a loss of CNS summation capacity (an electrophysiological measurement of nerve response) and an increase in blood cholinesterase activity in rats. No further details were provided. The study authors established the LOAEC and NOAEC at 6.6 and 0.8 mg/m^3, respectively, for the study. Due to limited information presented, the U.S. EPA considers this study inadequate to identify effect levels (U.S. EPA 2011).
    - Pregnant Sprague-Dawley rats (15/group) were exposed to 0, 9 or 18 mg/L n-butanol for 7 hours/day on gestational days 1 – 19 (maternal exposure group). Male Sprague-Dawley rats (18/group) were also exposed for 6 weeks and then mated to naïve females (paternal exposure group). Offspring were examined for neuromotor coordination, activity, learning and brain neurotransmitter analysis. Brain samples were taken to measure levels of total proteins and neurotransmitters. Exposure did not lead to any neurotoxicity to the offspring. The U.S. EPA established the NOAEC at 18 mg/L for this study.
  - ECETOC 2003
    - CNS depression observed with n-butanol administration is frequently recorded with most organic solvents at high levels. Additional data from well-designed neurotoxicity studies with n-butyl acetate which is rapidly cleaved into n-butanol do not indicate selective neuro- or CNS-related toxicity, but there were transient signs of reduced general activity at airborne levels of 1,500 and 3,000 ppm. In a well-designed developmental study following prenatal exposure of rats to n-butanol, no behavioral effects on the offspring were found. Therefore, it was concluded that n-butanol does not show selective or cumulative neurotoxicity in experimental animals.
    - In the occupational setting, chronic exposure of workers to high concentrations of n-butanol vapor was associated with CNS effects and hearing losses. However, these results must be interpreted with caution due to deficiencies in documentation and methodology of the studies. Therefore, no definitive conclusion could be drawn based on available data.

- ECHA 2014, U.S EPA 2011, ECETOC 2003, UNEP 2001
  - In a subchronic toxicity study, male Wistar rats (12/exposure group, 24 controls) were exposed to n-butanol at vapor concentrations of 0, 50 or 100 ppm (0, 154 or 308 mg/m^3, calculated by the document) for 6 h/day, 5 days/week for 3 months. Neuromuscular function (rotarod performance tests), learned avoidance behavior, and latency of the paw-lick response (hot-plate behavior) were examined. There were dose- and duration-related increases in the percentage of rotarod test failures but no effects on pain sensitivity (assessed by hot-plate behavior), and only the increased failure rates at the highest dose were statistically significant. U.S. EPA identified the NOAEC and LOAEC at 154 and 308 mg/m^3, respectively, based on

increased percentage of rotarod test failures. After adjustment for treatment frequency (i.e., 5 days/week -> 7 days/week), ToxServices calculated the NOAEC and LOAEC to be 110 and 220 mg/m^3 (equivalent to 0.11 and 0.22 mg/L, respectively[12]), respectively. The rotarod test is a test of motor function rather than memory or leaning that incorporates both central and peripheral nervous system components. It was assessed by evaluating the performance of the animal's performance on a rotarod prior to and at monthly intervals during the study. The U.S. EPA indicated that there are insufficient details presented by the authors on the rotarod test, such as number of rotarod trials per animal. ECHA and OECD assigned a Klimisch score of 3 (not reliable) for this study based on documentation insufficiency. ECETOC concluded from this study that n-butanol caused a moderate disturbance to co-ordination performance, which is a frequently observed unspecific solvent-related CNS effect. As such, these results did not indicate neurotoxicity in the sense of irreversible CNS or peripheral nervous system impacts. Further, the poorer performance on rotarod test in this study is questionable as the same authors identified the EC_{50} of more than 7,500 ppm for this test with a 4-h exposure to n-butanol. Korsak and Rydzynski 1994), and it could be deduced from this publication that exposure to concentrations of 2,500 ppm did not produce effects (MAK 2003). In the Korsak et al publication (1994), the study authors claimed to have trained the rats on the rotarod using the procedure of Kaplan and Murphy (1972), which described the challenge with this method including the constant daily training of the animals on the device. Korsak and colleagues did not maintain the training of the animals, but simply tested them every month without re-acclimating them to the rotarod method, which was inconsistent with the test implementation method recommended by the inventors of this method (i.e., Kaplan and Murphy). For this reason (improper use of the method), this study was considered invalid by the neurotoxicologists at the U.S. EPA Health Effects Research Laboratory (Eastman 2014). As the validity of this study is questionable, along with the other identified studies, data on the surrogate n-butyl acetate were therefore evaluated to support the safety of n-butanol.

- TSL 1995
    - n-Butyl acetate: In a GLP-compliant two-week inhalation probe study in rats, Sprague-Dawley rats (10/sex/dose) were exposed to n-butyl acetate vapor (99.9% pure) at 0, 750, 1,500 or 3,000 ppm for 6 hours/day, 6 days/week. Half of the animals at each dose were given food *ad libidum* while the other half were feed-restricted. Clinical signs of toxicity were monitored prior to exposure, during exposure and after exposure. In addition, an abbreviated functional observational battery (FOB) was performed prior to the first exposure and prior to necropsy. Exposure to n-butyl acetate gave rise to a concentration-related reduction in general activity levels during exposure, but without signs of toxicity after exposure. Animals appeared to acclimate to the 750 ppm concentrations, but not to 3,000 ppm. FOB test results did not show any treatment-related effects. The study authors established the NOAEC at 750 ppm (LOAEC 1,500 ppm) based on the acclimation

[12] mg/L is 1/1000 of mg/m^3. Therefore, the LOAEL of 220 mg/m^3 = 220 / 1,000 mg/L = 0.22 mg/L.

to exposure at this level (a NOEC cannot be determined). These concentrations are equivalent to 1.95 and 3.89 mg/L/6h/day, respectively[13].

- TSL 1996a, TSL 1996b, ECHA 2014
    - n-Butyl acetate: In a GLP-compliant subchronic inhalation toxicity study in rats, Sprague-Dawley rats (15/sex/dose) were exposed to n-butyl acetate vapor at 0, 500, 1,500 or 3,000 ppm for 6 hours/day, 5 days/week for 13 weeks. Acute but transient signs of reduced activity were observed at mid (minimal severity) and high doses (minor severity), demonstrated by less movement, decreased alertness and slower response to tapping on the chamber wall. These effects were also observed in the 13-week inhalation neurotoxicity study conducted by the same laboratory below, and the results are discussed in more details below.
    - n-Butyl acetate:– In a GLP-compliant subchronic inhalation neurotoxicity study in rats, Sprague-Dawley rats (10/sex/dose) were exposed to n-butyl acetate vapor at 0, 500, 1,500 or 3,000 ppm for 6 hours/day, 5 days/week for 13 weeks. Animals at each concentration were separated into two groups, one group was fed food *ad libidum* and designated for FOB, motor activity and neuropathology endpoints (FOB/MA/NP), and another group received restricted amount of food and were designated for schedule-controlled operant behavior (SCOB). At study termination, neurohistopathology was evaluated on randomly selected animals of control and high dose groups for the examination of brain (including forebrain, cerebrum, midbrain, cerebellum, pons, medulla oblongata), spinal cord swellings with dorsal and ventral roots (cervical and lumbar), dorsal root ganglia (cervical and lumbar), sciatic nerve (both hind limbs at mid-thigh and sciatic notch), and bitial nerve (both hind limbs including branches to the calf musculature). Acute but transient signs of reduced activity were observed at mid (minimal severity) and high doses (minor severity), demonstrated by less movement, decreased alertness and slower response to tapping on the chamber wall. No treatment-related effects were observed in FOB/MA/PA or SCOB. The study authors concluded that repeated exposure to n-butyl acetate vapors led to an acute, transient reduction of activity level on a daily basis at the mid and high doses, but no cumulative effects on activity were observed. Therefore, the authors established the NOEL for subchronic neurotoxicity at 3,000 ppm based on lack of cumulative neurotoxicity following repeated exposure. This is equivalent to 6.48 mg/L/6h/day n-butanol[14].
- All the neurotoxicity studies identified for n-butyl acetate were conducted under GLP. The TSL (1966b) inhalation neurotoxicity study comprehensively evaluated the neurotoxicity of n-butyl acetate and did not identify any adverse effects at the highest dose of 3,000 ppm (equivalent to 6.48 mg/L/6h/day n-butanol). Based on the weight of evidence, this study is selected as the critical study and the NOEL of 6.48 mg/L/6h/day is above the GHS category 2 cut-off value of 1 mg/L/6h/day for vapor.

Skin Sensitization (SnS) Group II* Score (H, M, or L): *L*

n-Butanol was assigned a score of Low for skin sensitization based on UNEP conclusion without data. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate data are

[13] Based on the equation of ppm = (MW x ppm ÷ 24,450) mg/L, 1,500 ppm n-butyl acetate = 1500 ppm n-butanol = (1,500 x 74 ÷ 24,450) mg/L = 4.54 mg/L/6h n-butanol. As animals were dosed 6 days per week, the mean daily dose = 4.54 mg/L x 6/7 = 3.89 mg/L/6h/day.

[14] Based on the equation of ppm = (MW x ppm ÷ 24,450) mg/L, 3000 ppm n-butyl acetate = 3000 ppm n-butanol = (3000 x 74 ÷ 24,450) mg/L = 9.08 mg/L/6h n-butanol. As animals were dosed 5 days per week, the mean daily dose = 9.08 mg/L x 5/7 = 6.49 mg/L/6h/day.

available and negative, there are no structural alerts, and they are not classified under GHS.

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists.
- No data were identified
- UNEP 2001
  - Although there are no animal data available, human studies and experience with n-butanol indicate that it is not likely to be a skin sensitizer

Respiratory Sensitization (SnR) Group II* Score (H, M, or L): DG

n-Butanol was assigned a score of data gap for respiratory sensitization based on lack of data for this endpoint.

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists.
- No data were identified

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M, or L): H

n-Butanol was assigned a score of High for skin irritation/ corrosivity based on experimental data and classification by authoritative and screening lists. GreenScreen® criteria classify chemicals as a High hazard for skin irritation when associated with EU R-phrase of R38 and H-Statement of H315 and when they are classified to GHS category 2 on a screening list (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* EU R38: Irritating to skin
  - *Authoritative:* EU H315: Causes skin irritation
  - *Screening:* GHS-Japan: Skin corrosion/irritation – Category 2
  - *Screening:* GHS-New Zealand: irritating to the skin– 6.3A
- UNEP 2001
  - Available animal data showed that n-butanol was non-irritating to moderately irritating to skin. Moderate skin irritation was seen in a 24-hour patch test where 405 or 500 mg of n-butanol was applied to the skin of rabbits (no further details provided).

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M, or L): vH

n-Butanol was assigned a score of Very High for eye irritation based on experimental data and on association with authoritative and screening lists. GreenScreen® criteria classify chemicals as a Very High hazard for eye irritation when associated with EU risk phrase of R41 and hazard statement of H318 (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* EU H318: Causes serious eye damage
  - *Authoritative*: EU R41: Risk of serious damage to eyes
  - *Screening:* GHS-Japan: Serious eye damage/eye irritation – Category 2A
  - *Screening:* GHS-New Zealand: Corrosive to ocular tissue – 8.3A
- UNEP 2001
  - The eye irritation potential of n-butanol was evaluated in rabbits. In studies in which 1.62 or 20 mg n-butanol was instilled into rabbit eyes, severe eye irritation occurred after 72 and 24 hours, respectively. In another study, 0.005 ml n-butanol instilled in rabbit eyes resulted in severe corneal irritation (no further details provided).

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): L
n-Butanol was assigned a score of Low for acute aquatic toxicity based on L/EC_{50} values being greater than 100 mg/L. GreenScreen® criteria classify chemicals as a Low hazard for acute aquatic toxicity when acute aquatic toxicity values are higher than 100 mg/L (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists.
- UNEP 2001, ECETOC 2003
  - LC_{50} = 1,376 – 2,300 mg/L in *Pimephales promela*s (fish, 96 hr)
  - EC_{50} = 1,328 – 1,983 mg/L in *Daphnia magn*a (invertebrates, 48 hr)
  - EC_{50} = 1,885 – 2,337 mg/L in *Daphnia magn*a (invertebrates, 24 hr)
  - EC_{50} = 1,900 – 2,300 in *Harpaticoid* (invertebrates, 96 hr)
  - EC_{50} > 500 mg/L in *Scenedesmus subspicatu*s (green algae, 96 hr)

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): *L*
n-Butanol was assigned a score of Low for chronic aquatic toxicity based on estimated chronic toxicity values being greater than 10 mg/L. GreenScreen™ criteria classify chemicals as a Low hazard for chronic aquatic toxicity when chronic aquatic toxicity values are greater than 10 mg/L (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists.
- UNEP 2001
  - No chronic toxicity data were identified. However, chronic toxicity values for fish (30-day ChV) and invertebrates (16- day EC_{50}) were estimated to be 72 and 21 mg/L, respectively by ECOSAR v. 0.99f. n-Butanol was designated to the neutral organics ECOSAR chemical class.

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): vL
n-Butanol was assigned a score of Very Low for persistence based on experimental data support this chemical being readily biodegradable within a 10-day window. GreenScreen® criteria classify chemicals as a Very Low hazard for persistence when adequate data are available and they are readily biodegradable within a 10-day window (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists.
- UNEP 2001
  - Several studies have been conducted to assess the biodegradation of n-butanol in water and treated Sewage under aerobic conditions. In these studies, n-butanol was considered readily biodegradable; 88% degradation within 30 days in a closed bottle test; 98% degradation within 14 days in an OECD-screening test; 100% degraded in 5 days in a Zahn-Wellens test; 98.5% degradation in a Coupled Units test; rapid biodegradation within a few days in a number of other studies.

- U.S. EPA 2012
    - The BIOWIN modeling Ready Biodegradable Predictor indicates that n-butanol is expected to be readily biodegradable. Fugacity modeling predicts 55.2% will partition to soil with a half-life of 17.3 days, 40.1% will partition to water with a half-life of 8.7 days, and 4.56% will partition to air with a half-life of 1.25 days.
- Based on the weight of evidence, a score of Very Low was assigned. Fugacity modeling predicts that n-butanol will partition primarily to soil. n-Butanol was readily biodegradable and meets the 10-day window. When the major compartment is soil, GreenScreen® criteria specify a score of Very Low if the chemical meets the 10-day window in a ready biodegradation test.

Bioaccumulation (B) Score (vH, H, M, L, or vL): *vL*
n-Butanol was assigned a score of Very Low for bioaccumulation based on its estimated BCF of 3 in fish. GreenScreen™ criteria classify chemicals as a Very Low hazard for bioaccumulation when BCFs/BAFs are less than100 (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists.
    - *Screening:* Not listed on any screening lists.
- UNEP 2001
    - An estimated BCF of 3 was calculated in fish for n-butanol, using a log K_{ow} of 0.88 with EPISUITE (v. 3.10) and BCFWOM (v. 2.14). According to GHS criteria, this BCF suggests the potential for bioconcentration in aquatic organisms is low.

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): L
n-Butanol was assigned a score of Low for reactivity based on not having any chemicals or functional groups expected to contain high energy bonds or oxidizing species which may cause reactivity. This chemical would not be classified for reactivity under GHS (UN 2013). GreenScreen® criteria classify chemicals as a Low hazard for reactivity when it is not explosive, unless there are data showing otherwise (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* not listed in any authoritative lists
    - *Screening:* not listed in any screening lists
- ECHA 2014
    - n-Butanol would not be classified as an oxidizing chemical as it does not contain structural groups that would cause concern for explosion (is not associated with any relevant EU hazard statements).

Flammability (F) Score (vH, H, M, or L): H
n-Butanol was assigned a score of High for flammability based on a flash point being between 23- 60 ^{0}C and on association with authoritative lists. GreenScreen® criteria classify chemicals as a High hazard for flammability when associated with DOT Class 2, Group 2 classification and when adequate data are available and they are classified to GHS category 3 for flammable liquid (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* EU H226: Flammable liquid and vapor
    - *Authoritative:*WHMIS: Class B2 – Flammable liquids
    - *Authoritative:*DOT: Class 3, Group 2 – Flammable liquid
    - *Screening:* Not listed in any screening lists.

    - *Others:* Japan-GHS: Flammable liquids - Category 3
    - *Others* New Zealand -GHS: Flammable Liquids: medium hazard - 3.1C
- UNEP 2001
    - n-Butanol has a flammable range of 1.4 – 11.2 volume % in air (14,000 – 112,000 ppm) and a flash point of 98^{o}F (37^{o}C).
- Based on the available data, n-butanol is classified to GHS category 3 for flammable liquids (liquids which have a flash point of between 23^{o}C and 60^{o}C).

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APPENDIX A: Hazard Benchmark Acronyms
(in alphabetical order)

(AA) Acute Aquatic Toxicity

(AT) Acute Mammalian Toxicity

(B) Bioaccumulation

(C) Carcinogenicity

(CA) Chronic Aquatic Toxicity

(Cr) Corrosion/ Irritation (Skin/ Eye)

(D) Developmental Toxicity

(E) Endocrine Activity

(F) Flammability

(IrE) Eye Irritation/Corrosivity

(IrS) Skin Irritation/Corrosivity

(M) Mutagenicity and Genotoxicity

(N) Neurotoxicity

(P) Persistence

(R) Reproductive Toxicity

(Rx) Reactivity

(SnS) Sensitization- Skin

(SnR) Sensitization- Respiratory

(ST) Systemic/Organ Toxicity

APPENDIX B: Results of Automated GreenScreen® Score Calculation for n-Butanol (CAS # 71-36-3)

TOXSERVICES TOXICOLOGY RISK ASSESSMENT CONSULTING

GREEN SCREEN FOR SAFER CHEMICALS

GreenScreen® Score Inspector

Table 1: Hazard Table

			Group I Human					Group II and II* Human								Ecotox		Fate		Physical	
			Carcinogenicity	Mutagenicity/Genotoxicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
Table 2: Chemical Details									S	R *	S	R *	*	*								
Inorganic Chemical?	Chemical Name	CAS#	C	M	R	D	E	AT	STs	STr	Ns	Nr	SNS*	SNR*	IrS	IrE	AA	CA	P	B	Rx	F
No	n-Butanol	71-36-3	*L*	L	L	L	DG	M	M	L	DG	L	*L*	DG	H	vH	L	L	vL	*vL*	*L*	H

Table 3: Hazard Summary Table

Benchmark	a	b	c	d	e	f	g
1	No	No	No	No	No		
2	No	No	No	No	No	Yes	Yes
3	STOP						
4	STOP						

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
n-Butanol	2

Note: Chemical has not undergone a data gap assessment. Not a Final GreenScreen™ Score

Table 6

Chemical Name	Final GreenScreen® Benchmark Score
n-Butanol	2

After Data gap Assessment
Note: No Data gap Assessment Done if Preliminary GS Benchmark Score is 1.

Table 5: Data Gap Assessment Table

Datagap Criteria	a	b	c	d	e	f	g	h	i	j	bm4	End Result
1												
2	Yes	Yes	Yes	Yes	Yes							2
3												
4												

APPENDIX C: Pharos Output for n-Butanol (CAS # 71-36-3)

N-BUTANOL

CAS RN: 71-36-3

Synonyms: Butanol; N-Butyl Alcohol; 1-butanol

Detailed Direct Hazard Listings — Quickscreen

MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Specific target organs/systemic toxicity following repeated exposure - Category 1 - GreenScreen Benchmark Unspecified (LT-U)
EYE IRRITATION	EC - CLP/GHS Hazard Statements (EU H-Statements) H318 Causes serious eye damage - GreenScreen Benchmark Unspecified (LT-U) - HPD
EYE IRRITATION	EC - Risk Phrases (EU R-Phrases) R41: Risk of serious damage to eyes. - GreenScreen Benchmark Unspecified (LT-U) - HPD
EYE IRRITATION	New Zealand HSNO/GHS (GHS-New Zealand) 8.3A - Corrosive to ocular tissue - GreenScreen Benchmark Unspecified (LT-U)
EYE IRRITATION	Japan METI/MOE - GHS Classifications (GHS-Japan) Serious eye damage / eye irritation - Category 2A - GreenScreen Benchmark Unspecified (LT-U)
CANCER	US EPA - IRIS Carcinogens (EPA-C) (1986) Group D - Not classifiable as to human carcinogenicity - Not included in GreenScreen
DEVELOPMENTAL	German MAK - List of Substances (MAK) Pregnancy Risk Group C - GreenScreen Benchmark Unspecified (LT-U)
RESPIRATORY	EC - Risk Phrases (EU R-Phrases) R37: Irritating to respiratory system. - GreenScreen Benchmark Unspecified (LT-U)
NEUROTOXICITY	EC - Risk Phrases (EU R-Phrases) R67: Vapours may cause drowsiness and dizziness - GreenScreen Benchmark Unspecified (LT-U)
NEUROTOXICITY	EC - CLP/GHS Hazard Statements (EU H-Statements) H336 May cause drowsiness or dizziness - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	EC - Risk Phrases (EU R-Phrases) R22: Harmful if swallowed. - GreenScreen Benchmark Unspecified (LT-U) - HPD
MAMMALIAN	EC - CLP/GHS Hazard Statements (EU H-Statements) H302 Harmful if swallowed - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Québec CSST - WHMIS Classifications (WHMIS) Class D2B - Toxic material causing other toxic effects - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	New Zealand HSNO/GHS (GHS-New Zealand) 6.1D (oral) - Acutely toxic - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Acute toxicity (dermal) - Category 5 - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Acute toxicity (oral) - Category 4 - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Specific target organs/systemic toxicity following single exposure - Category 3 - GreenScreen Benchmark Unspecified (LT-U)
SKIN IRRITATION	EC - Risk Phrases (EU R-Phrases) R38: Irritating to skin. - GreenScreen Benchmark Unspecified (LT-U) - HPD
SKIN IRRITATION	EC - CLP/GHS Hazard Statements (EU H-Statements) H315 Causes skin irritation - GreenScreen Benchmark Unspecified (LT-U) - HPD

SKIN IRRITATION	Japan METI/MOE - GHS Classifications (GHS-Japan) Skin corrosion / irritation - Category 2 - GreenScreen Benchmark Unspecified (LT-U)
ORGAN TOXICANT	EC - CLP/GHS Hazard Statements (EU H-Statements) H335 May cause respiratory irritation - GreenScreen Benchmark Unspecified (LT-U)
TERRESTRIAL	New Zealand HSNO/GHS (GHS-New Zealand) 9.3C - Harmful to terrestrial vertebrates - Not included in GreenScreen
FLAMMABLE	EC - CLP/GHS Hazard Statements (EU H-Statements) H226 Flammable liquid and vapour - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only
FLAMMABLE	Québec CSST - WHMIS Classifications (WHMIS) Class B2 - Flammable liquids - GreenScreen Benchmark Unspecified (LT-U)
FLAMMABLE	New Zealand HSNO/GHS (GHS-New Zealand) 3.1C - Flammable Liquids: medium hazard - GreenScreen Benchmark Unspecified (LT-U)
FLAMMABLE	Japan METI/MOE - GHS Classifications (GHS-Japan) Flammable liquids - Category 3 - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	New Zealand HSNO/GHS (GHS-New Zealand) 6.1E (dermal) - Acutely toxic - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	New Zealand HSNO/GHS (GHS-New Zealand) 6.1E (inhalation) - Acutely toxic - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Aspiration hazard - Category 2 - Not included in GreenScreen - occupational hazard only
FLAMMABLE	EC - Risk Phrases (EU R-Phrases) R10: Flammable LIQUID - Not included in GreenScreen
RESTRICTED LIST	German FEA - Substances Hazardous to Waters (VwVwS) Class 1 Low Hazard to Waters - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only

Lifecycle Hazard Quickscreen

Full Lifecycle Map

Research Status: Preliminary literature review drafted
The Pharos team has undertaken a preliminary literature review of some of the processes involved in the manufacture of this substance and identified the following chemicals. This list of chemicals is not exhaustive of all chemicals that may be involved in the production or life cycle of this substance.

May contain residual manufacturing chemicals that have a hazard of...

Comes from additional manufacturing chemicals that have a hazard of...

PBT	Alcohol [64-17-5] - Frequent Feedstock
CANCER	Alcohol [64-17-5] - Frequent Feedstock
DEVELOPMENTAL	Alcohol [64-17-5] - Frequent Feedstock
REPRODUCTIVE	Alcohol [64-17-5] - Frequent Feedstock
GENE MUTATION	Alcohol [64-17-5] - Frequent Feedstock
RESPIRATORY	ACETALDEHYDE [75-07-0] - Frequent Intermediate
NEUROTOXICITY	ACETALDEHYDE [75-07-0] - Frequent Intermediate
MAMMALIAN	Alcohol [64-17-5] - Frequent Feedstock
EYE IRRITATION	ACETALDEHYDE [75-07-0] - Frequent Intermediate
SKIN IRRITATION	BUTYRALDEHYDE [123-72-8] - Frequent Feedstock
ORGAN TOXICANT	BUTYRALDEHYDE [123-72-8] - Frequent Feedstock
ACUTE AQUATIC	ACETALDEHYDE [75-07-0] - Frequent Intermediate
TERRESTRIAL	BUTYRALDEHYDE [123-72-8] - Frequent Feedstock
FLAMMABLE	BUTYRALDEHYDE [123-72-8] - Frequent Feedstock
REACTIVE	ACETALDEHYDE [75-07-0] - Frequent Intermediate
RESTRICTED LIST	BUTYRALDEHYDE [123-72-8] - Frequent Feedstock

VOC designation: VOC (Boiling point: 118 degrees Celsius)

Pharos Team Notes:

N-butyl alcohol " is employed as a solvent for paints, lacquers & varnishes, natural & synthetic resins, gums, vegetable oils, dyes & alkaloids. It is used as an intermediate in the manufacture of pharmaceuticals & chemicals, & employed in industries producing artificial leather, textiles, safety glass, rubber cement, shellac, raincoats, photographic films & perfumes." [International Labour Office. Encyclopaedia of Occupational Health and Safety. 4th edition, Volumes 1-4 1998. Geneva, Switzerland: International Labour Office, 1998., p. 104.32]

APPENDIX D: EPISuite Modeling Results for n-Butanol (CAS # 71-36-3)

CAS Number: 71-36-3
SMILES : C(CC)CO
CHEM : n-butanol
MOL FOR: C4 H10 O1
MOL WT : 74.12
---------- EPI SUMMARY (v4.11) ----------

Physical Property Inputs:
Log Kow (octanol-water): 0.88
Boiling Point (deg C) : ------
Melting Point (deg C) : -89.80
Vapor Pressure (mm Hg) : 6.7
Water Solubility (mg/L): 63.2
Henry LC (atm-m3/mole) : ------

Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.68 estimate) = 0.84
Log Kow (Exper. database match) = 0.88
Exper. Ref: HANSCH,C ET AL. (1995)

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 113.91 (Adapted Stein & Brown method)
Melting Pt (deg C): -62.33 (Mean or Weighted MP)
VP(mm Hg,25 deg C): 7.78 (Mean VP of Antoine & Grain methods)
VP (Pa, 25 deg C) : 1.04E+003 (Mean VP of Antoine & Grain methods)
MP (exp database): -89.8 deg C
BP (exp database): 118 deg C
VP (exp database): 6.70E+00 mm Hg (8.93E+002 Pa) at 25 deg C

Water Solubility Estimate from Log Kow (WSKOW v1.42):
Water Solubility at 25 deg C (mg/L): 8.117e+004
log Kow used: 0.88 (user entered)
melt pt used: -89.80 deg C
Water Sol (Exper. database match) = 6.32e+004 mg/L (25 deg C)
Exper. Ref: TEWARI,YB ET AL. (1982)

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 61389 mg/L

ECOSAR Class Program (ECOSAR v1.11):
Class(es) found:
Neutral Organics

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method : 9.99E-006 atm-m3/mole (1.01E+000 Pa-m3/mole)
Group Method: 9.74E-006 atm-m3/mole (9.87E-001 Pa-m3/mole)
Exper Database: 8.81E-06 atm-m3/mole (8.93E-001 Pa-m3/mole)

For Henry LC Comparison Purposes:
User-Entered Henry LC: not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC: 1.034E-002 atm-m3/mole (1.048E+003 Pa-m3/mole)
VP: 6.7 mm Hg (source: User-Entered)
WS: 63.2 mg/L (source: User-Entered)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
Log Kow used: 0.88 (user entered)
Log Kaw used: -3.443 (exp database)
Log Koa (KOAWIN v1.10 estimate): 4.323
Log Koa (experimental database): 4.190

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model) : 0.9794
Biowin2 (Non-Linear Model) : 0.9927
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 3.4937 (days-weeks)
Biowin4 (Primary Survey Model) : 4.1393 (days)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model) : 0.8014
Biowin6 (MITI Non-Linear Model): 0.9369
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): 0.6495
Ready Biodegradability Prediction: YES

Hydrocarbon Biodegradation (BioHCwin v1.01):
Structure incompatible with current estimation method!

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled): 893 Pa (6.7 mm Hg)
Log Koa (Exp database): 4.190
Kp (particle/gas partition coef. (m3/ug)):
Mackay model : 3.36E-009
Octanol/air (Koa) model: 3.8E-009
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model : 1.21E-007
Mackay model : 2.69E-007
Octanol/air (Koa) model: 3.04E-007

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 6.8900 E-12 cm3/molecule-sec
Half-Life = 1.552 Days (12-hr day; 1.5E6 OH/cm3)
Half-Life = 18.629 Hrs
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
1.95E-007 (Junge-Pankow, Mackay avg)

3.04E-007 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):
Koc : 3.471 L/kg (MCI method)
Log Koc: 0.540 (MCI method)
Koc : 10.01 L/kg (Kow method)
Log Koc: 1.000 (Kow method)
Experimental Log Koc: 0.5 (database)

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
Rate constants can NOT be estimated for this structure!

Bioaccumulation Estimates (BCFBAF v3.01):
Log BCF from regression-based method = 0.500 (BCF = 3.162 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -1.1665 days (HL = 0.06816 days)
Log BCF Arnot-Gobas method (upper trophic) = 0.169 (BCF = 1.475)
Log BAF Arnot-Gobas method (upper trophic) = 0.169 (BAF = 1.475)
log Kow used: 0.88 (user entered)

Volatilization from Water:
Henry LC: 8.81E-006 atm-m3/mole (Henry experimental database)
Half-Life from Model River: 58.09 hours (2.421 days)
Half-Life from Model Lake : 705.9 hours (29.41 days)

Removal In Wastewater Treatment:
Total removal: 2.36 percent
Total biodegradation: 0.09 percent
Total sludge adsorption: 1.78 percent
Total to Air: 0.49 percent
(using 10000 hr Bio P,A,S)

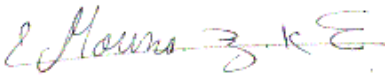
Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	4.56	30	1000
Water	40.1	208	1000
Soil	55.2	416	1000
Sediment	0.0747	1.87e+003	0

Persistence Time: 240 hr

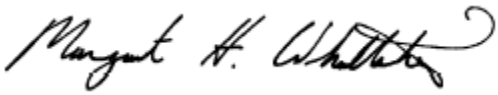
Authorized Reviewers

n-Butanol GreenScreen® Evaluation Prepared By:



Mouna Zachary, Ph.D.
Toxicologist
ToxServices LLC

n-Butanol GreenScreen® Evaluation QC'd By:



Margaret H. Whittaker, Ph.D., M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Managing Director and Chief Toxicologist
ToxServices LLC