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Content Copyright 2014 ©: Alex Stone: n-Propyl bromide (CAS Nr. 106-94-5)

GreenScreen® Assessment for n-Propyl Bromide (nPB) (CAS # 106-94-5)

Method Version: GreenScreen® Version 1.2[1]

Assessment Type[2]: Authorized GreenScreen Practitioner

GreenScreen® Assessment Prepared By:	GreenScreen® Assessment Quality Control Performed By:
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Organization: Washington State Department of Ecology	Organization: Rosenblum Environmental consulting to Clean Production Action
Date: 12/3/2014	Date: 5/1/2015
Assessor Type: Certified practitioner	

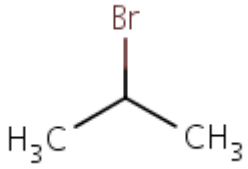
Confirm application of the *Disclosure and Assessment Rules and Best Practice*[3]: (List disclosure threshold and any deviations)

Chemical Name (CAS #): n-Propyl bromide (nPB) (106-94-5)

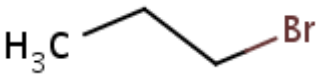
Also Called: Propane, 1-bromo-; propyl bromide; 1-BP; CCRIS 30; UNII-Y9746DNE68, 1-bromopropane

Suitable analogs or moieties of chemicals used in this assessment:

Analog: 2-Bromopropane (CAS # 75-26-3)



Chemical Structure:
nPB (CAS # 106-94-5)



Smiles:

[1] Use GreenScreen® Assessment Procedure (Guidance) V1.2
[2] GreenScreen reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen Practitioner), "CERTIFIED" (by Licensed GreenScreen Profiler or equivalent) or "CERTIFIED WITH VERIFICATION" (Certified or Authorized assessment that has passed GreenScreen Verification Program)
[3] See GreenScreen Guidance V1.2

*Note: Include chemical structure(s) of all suitable analogs (and /or moieties) used in the assessment.

Notes related to production specific attributes[4]:

For Inorganic Chemicals and relevant particulate organics (*if not relevant, list NA*)
Define Properties:

1. Particle size (e.g., silica of respirable size): NA
2. Structure (e.g., amorphous vs. crystalline): NA
3. Mobility (e.g., water solubility, volatility): NA
4. Bioavailability: '*No human kinetic or metabolism data were identified. Empirical evidence from rodent studies indicates that 1-BP is absorbed by the inhalation route. However, animal studies that characterize and quantify absorption and distribution of 1-BP by any route were not found.*' (CERHR, 2003)

Identify Applications/Functional Uses: (e.g. Cleaning product, TV casing)

1. Solvent for fats, waxes and resins.
2. Production of penconazole (fungicide), valproic acid (anticonvulsant and mood-stabilizing drug).
3. In the early to mid 1990s, used primarily as an intermediate in the production of pesticides, quaternary ammonium compounds, flavors and fragrances, pharmaceuticals, and other chemicals in well-controlled, closed processes.
4. In the mid to late 1990s, introduced as a less toxic replacement for methylene chloride in emissive applications such as vapor and immersion degreasing operations and critical cleaning of electronics and metals.
5. Non-flammable, non-toxic, fast-drying, and inexpensive solvent for adhesive resins
6. Marketed as a replacement for ozone depleting refrigerants.
7. Intermediate in the production of Albendazole, an anthelmintic (drugs that expel parasitic worms and other internal parasites from the body without causing damage to the host) against nematode infections.
8. Vapor and immersion degreasing operations for cleaning metals, plastics and electronic and optical components.
9. Adhesive spray applications.
10. Dry cleaning.
11. Solvent sprays used in operations like asphalt production, aircraft maintenance, and synthetic fiber manufacturing.

[4] Note any composition or hazard attributes of the chemical product relevant to how it is manufactured. For example, certain synthetic pathways or processes result in typical contaminants, by-products or transformation products. Explain any differences between the manufactured chemical product and the GreenScreen assessment of the generic chemical by CAS #.

Introduction

1-Bromopropane is a clear, colorless liquid with a sweet odor. It is used in dry cleaning, and as a solvent, adhesive, and an aerosol propellant. (NJDOH, 2009)

It is created by treating the parent hydroxyl compound with a bromide and sulfuric acid as in the preparation of methyl bromide. If the parent compound is unstable toward sulfuring acid, hydrobromic acid is passed in and alkyl bromide is flashed over from the hot mixture. The product is condensed, neutralized, and fractionated. In modification of these procedures, bromine may be used along with a reducing agent such as sulfur, sulfur dioxide, phosphorous or sodium borohydride. (HSDB, 2015)

At least three manufacturers are limiting or eliminating use of nPB for solvent applications. Great Lakes Chemical no longer sells nPB solvent blends. ATOFINA has decided not to market it for solvent applications. Albemarle has stated that use of nPB in adhesive and other applications in which exposure cannot be controlled should be restricted or prohibited. (CERHR, 2003).

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GreenScreen Benchmark Score and Hazard Summary Table:[5,6,7,8] nPB was assigned a **Benchmark Score of 1** based on identification as a carcinogenic, reproductive and developmental toxicant (1e). These conclusions may change if new data is found for the hazard criteria based upon new or additional analytical studies.

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*										
H	**L**	**H**	**H**	DG	**M**	**M**	*M*	*M*	**M**	*L*	DG	**H**	**H**	**M**	*M*	*H*	*vL*	**M**	**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 or L) instead of three (i.e., H, M or L), and are based on single exposures instead of repeated exposures.

[5] See Appendix A for a glossary of hazard endpoint acronyms
[6] See Appendix B for alternative GreenScreen Hazard Summary Table (Classification presented by exposure route)
[7] For inorganic chemicals only, see GreenScreen Guidance V1.2 Section 14.4. (Exceptions for Persistence)
[8] For Systemic Toxicity and Neurotoxicity, repeated exposure data are preferred. Lack of single exposure data is not a Data Gap when repeated exposure data are available. In that case, lack of single exposure data may be represented as NA instead of DG. See GreenScreen Guidance V1.2 Section 9.3.

Environmental Transformation Products and Ratings[9]:

Identify feasible and relevant environmental transformation products (i.e., dissociation products, transformation products, valence states) and/or moieties of concern[10]

Functional Use	Life Cycle Stage	Transformation Pathway	Environmental Transformation Products	CAS #	Feasible and Relevant?	GreenScreen List Translator or Benchmark Score
N/A	End of life	Hydrolysis	1-bromo-2-propanol	19686-73-8	Yes	N/A
N/A	End of life	Hydrolysis	bromoacetone	598-31-2	Yes	LT-UNK
N/A	End of life	Hydrolysis	Hydrogen bromide	10035-10-6	Yes	LT-UNK

[9] See GreenScreen Guidance V1.2 Section 13
[10] 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.

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

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

nPB was assigned a score of **HIGH** for carcinogenicity based on determination by two authoritative sources, the NIH's Report on Carcinogens and the German MAK as sufficiently carcinogenic to warrant the high level of concern. These results were supported by two two-year carcinogenicity studies reported by the European Chemicals Agency (ECHA). As the level of concern is based upon authoritative sources and analytical data, it is bolded in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:*
    - US NIH - Report on Carcinogens - Reasonably Anticipated to be Human Carcinogen (Pharos)
    - German MAK - List of Substances - Carcinogen Group 2 - Considered to be carcinogenic for man (Pharos)
  - *Screening:*
    - US EPA - PPT Chemical Action Plans - Possible carcinogen - TSCA Criteria met (Pharos)

- European Chemicals Agency (ECHA), 2015
  - Results: Some evidence of carcinogenic activity including rare adenomas of the large intestine, increased incidences of skin neoplasms, malignant mesotheliomas and pancreatic islet adenoma.
    Species: Rats.
    Exposure route: Not stated although assume inhalation.
    Method: OECD Guideline 453 (Combine Chronic Tox./Carcinogenicity Studies), 2011.
    Reliability: Reliable without restriction - Study conducted in compliance with agreed protocols, with no or minor deviations from standard test guidelines and/or minor methodological deficiencies, which do not affect the quality of the relevant results. The study report was conclusive, done to a valid guidelines and the study was conducted under GLP conditions.

  Under the conditions of this 2-year inhalation study, there was some evidence of carcinogenic activity of 1-bromopropane in male F344/N rats based on the occurrence of rare adenomas of the large intestine and increased incidences of neoplasms of the skin. Increased incidences of malignant mesothelioma and pancreatic islet adenoma may also have been related to 1-bromopropane exposure. There was clear evidence of carcinogenic activity of 1-bromopropane in female F344/N rats based on increased incidences of adenoma of the large intestine. Increased incidences of neoplasms of the skin may also have been related to 1-bromopropane exposure. Exposure to 1-bromopropane resulted in increased

incidences of non-neoplastic lesions in the nose of rats, the larynx of rats, and the trachea of female rats. Suppurative inflammatory lesions with Splendore-Hoeppli material were present primarily in the nose and skin of male and female rats exposed to 1-bromopropane.

- Results: Clear evidence of carcinogenic activity (female) including alveolar/bronchiolar neoplasms and non-neoplastic lesions in the nose, trachea and lungs and larynx.
  Species: Mice
  Exposure route: Inhalation.
  Method: OECD Guideline 453 (Combine Chronic Tox./Carc. Studies), 2003-05.
  Reliability: Reliable without restriction - Study conducted in compliance with agreed protocols, with no or minor deviations from standard test guidelines and/or minor methodological deficiencies, which do not affect the quality of the relevant results. The study report was conclusive, done to a valid guidelines and the study was conducted under GLP conditions.

Under the conditions of this 2-year inhalation study, there was no evidence of carcinogenic activity of 1-bromopropane in male B6C3F1 mice exposed to concentrations of 62.5, 125, or 250 ppm 1-bromopropane. There was clear evidence of carcinogenic activity of 1-bromopropane in female B6C3F1 mice based on increased incidences of alveolar/bronchiolar neoplasms. Exposure to 1-bromopropane resulted in increased incidences of non-neoplastic lesions in the nose, trachea and lungs of all mice and the larynx of male mice.

Data Summary:

nPB was identified by an authoritative source, the NIH Report on Carcinogens, to be 'reasonably anticipated to be a human carcinogen' which equates to a high level of concern in the GreenScreen criteria. This determination was supported by the German MAK which assigned nPB a Category 2 (equates to GreenScreen high) level of concern and by the EPA which identified it as a possible carcinogen in its Chemical Action Plan. EPA's Chemical Action Plans are not currently referenced in GreenScreen criteria but is used to support other results.

In addition, the European Chemical Agency (ECHA) reported two two-year carcinogenic studies which indicated some and clear evidence of carcinogenic activity, respectively. Impacts included rare adenomas of the large intestine, increased incidences of skin neoplasms, malignant mesotheliomas and pancreatic islet adenoma and alveolar/bronchiolar neoplasms and non-neoplastic lesions in the nose, trachea and lungs and larynx.

For these reasons, nPB is assigned a score of HIGH for carcinogenicity.

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

nPB was assigned a score of **LOW** level of concern for mutagenicity based on several laboratory studies using a variety of animal and plant species that indicated nPB was non-mutagenic. One study did indicate some mutagenic concern; however, additional studies using the same test

species did not indicate any mutagenicity. As the low level of concern is based upon laboratory results, it is bolded in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:* None
  - *Screening:* None

- NIH National Library of Medicine Hazardous Substances Databank
  - Results: Mutagenic with or without activation for two specie strains.
    Species: Salmonella typhimurium.
    Exposure route: Not stated other than 'closed system'.
    Method: Not stated.
    Reliability: Not stated.

    '*1-BP was mutagenic with or without metabolic activation toward Salmonella typhimurium tester strains TA1535 and TA100 when tested in a closed system, but it was not mutagenic toward strains TA1537, TA1538, or TA98.*'

  - Results: Not mutagenic.
    Species: Rats.
    Exposure route: Oral.
    Method: Not stated.
    Reliability: Not stated.

    '*1-BP did not induce dominant lethal mutations in Sprague-Dawley rats given 400 mg/kg by oral gavage for 5 days.*'

  - Results: Not mutagenic.
    Species: Salmonella typhimurium and E. Coli.
    Exposure route: Oral.
    Method: Not stated.
    Reliability: Not stated.

    '*1-Bromopropane was not mutagenic in either of two independent bacterial mutagenicity assays, each conducted with and without induced rat liver activation enzymes. Bacterial strains tested included Salmonella typhimurium strains TA97, TA98, TA100, and TA1535, and Escherichia coli strain WP2 uvrA/pKM101. In addition, no increases in the frequencies of micronucleated normochromatic erythrocytes were seen in male or female B6C3F1 mice exposed for 3 months to 62.5 to 500 ppm 1-bromopropane via inhalation.*'

  - Results: Not mutagenic.
    Species: Rats.
    Exposure route: Inhalation.
    Method: Micronucleus assay, more information not stated.
    Reliability: Not stated.

'*...A micronucleus assay was conducted by exposing 10 Sprague-Dawley rats/sex/group to 0, 50, 300, or 1,800 ppm [0, 252, 1,509, or 9,055 mg/cu m] 1-BP vapors for 6 hr/day, 5 days/wk, for 8 weeks. After treatment was complete, the rats were sacrificed and bone marrow was examined to determine the frequency of micronucleated polychromatic erythrocytes. 1-BP treatment did not increase the frequency of micronucleated polychromatic erythrocytes.*'

- Results: Not mutagenic.
  Species: Mice bone marrow cells.
  Exposure route: Oral.
  Method: Micronucleus assay, more information not stated.
  Reliability: Not stated.

'...A micronucleus study of 1-BP in bone marrow of mice was conducted. In the initial study, male and female Swiss OF1/ICO:OF1 (IOPS Caw) mice ... were treated twice with 0, 100, 400, or 800 mg/kg 1-BP (99.3%) in corn oil by ip injection. Cyclophosphamide was used as a reference clastogen. At least 5 animals/sex/group were used. Animals were killed 24 hours after the last treatment. The initial toxicity study indicated that 800 mg/kg would be a suitable high dose, and a second study was conducted with 0 and 800 mg/kg 1-BP. Mortality in males during the second study prompted a third study using an additional dose level of 600 mg/kg for males. Only the 600 mg/kg males and 800 mg/kg females were evaluated because the polychromatic/normochromatic erythrocyte (PE/NE) ratio for the controls from the initial attempt (100, 400, 800 mg/kg) were outside of the historic range and the test was considered invalid. No increase in micronucleated erythrocytes in bone marrow was observed in males treated with 600 mg/kg or in females treated with 800 mg/ kg. The group treated with cyclophosphamide demonstrated a significant increase in micronucleated erythrocytes.'

- Results: Not mutagenic.
  Species: Mouse lymphoma cells.
  Exposure route: Screening study, intraperitoneal injection, subsequent studies, not stated.
  Method: Not stated.
  Reliability: Not stated.

'...The mutagenicity of 1-BP in L5178Y mouse lymphoma cells was examined/. The cells were treated for 3 hours with 125-1,500 mg/L 1-BP (99.3% purity) in the absence of metabolic activation or 125-2,500 mg/L 1-BP with S9 (from rats treated with Aroclor 1254) activation. The vehicle, DMSO, was used as a negative control. Methylmethane sulfonate and cyclophosphamide were used as reference mutagens. The highest concentration (2,500 mg/L) produced 100% cytolethality while the 2,000 mg/L concentration produced /about/ 40-90% cytolethality, as assessed by relative cloning efficiency. A reproducible two-fold increase in mutation frequency compared to the concurrent control and/or evidence of a dose relationship were considered indicative of a positive response. Two separate experiments were conducted. In the absence of metabolic activation, a reproducible increase in mutation frequency was observed in cells treated with 1,000-1,500 mg/L 1-BP in both experiments. No increase in mutation frequency was observed in the first experiment with S9 activated cells.

However, in the second experiment with S9 activated cells, an increase in mutation frequency was noted at 1,500-2,000 mg/L 1-BP. Study authors concluded that this study demonstrated mutagenic activity, especially in the absence of S9 activation.'

- ECHA, 2015.
  - Results: Not genotoxic, with or without metabolic activation.
    Species: Salmonella typhimurium.
    Exposure route: Dissolved and diluted in dimethyl sulfoxide.
    Method: Ames test, OECD Guideline 471 (Bacterial Reverse Mutation Assay), 1993.
    Reliability: Reliable without restriction - Study conducted in compliance with agreed protocols, with no or minor deviations from standard test guidelines and/or minor methodological deficiencies, which do not affect the quality of the relevant results.

  The genotoxic potential of nPB was assessed by the Ames test on five Salmonella typhimurium tester strains: TA1353, TA1537, TA1538, TA98 and TA100, both in the absence and presence of metabolic activation. nPB was dissolved and diluted in dimethyl sulfoxide and tested at concentrations ranging from 100 to 10,000 µg/plate. During the first genotoxicity study (HIS1005) performed at 100, 500, 1000, 5000 and 10,000 µg/plate, a slight toxic effect was observed mainly at 10,000 µg/plate on the five tester strains with S9 mux and in TA1535, TA 1538, TA98 and TA100 without S9 mix. A second study (HIS1005A) performed at the same concentrations confirmed these results. In both studies, whether in the presence or in the absence of metabolic activation, no increase was observed in the number of His+ revertant colonies/plate at any of the concentrations tested, on the five tester strains, with and without S9 mix. In conclusion, nPB was not genotoxic in the Ames test, with or without metabolic activation.

  - Results: Not genotoxic.
    Species: Mice erythrocytes.
    Exposure route: Inhalation.
    Method: OECD Guideline 474 (Mammalian Erythrocyte Micronucleus Test).
    Reliability: Reliable without restriction - Study conducted in compliance with agreed protocols, with no or minor deviations from standard test guidelines and/or minor methodological deficiencies, which do not affect the quality of the relevant results.

  No increases in the frequencies of micronucleated normochromatic erythrocytes were seen in male or female B6C3F1 mice exposed for 3 months to 62.5 to 500 ppm 1-bromopropane via inhalation. The percentage of reticulocytes (polychromatic erythrocytes) in the peripheral blood of male and female mice was unaltered by 1-bromopropane exposure, suggesting a lack of chemical-associated bone marrow toxicity.

Data Summary:

nPB was assigned a score of LOW for mutagenicity based on test results for a wide range of test media including salmonella strains, mice erythrocytes, mice bone marrow and rats and, in several cases, with or without metabolic activation. One study did report mutagenicity in two salmonella strains, specifically TA1535 and TA100. Other studies, however, using the same strains did not

report any mutagenicity. In addition, tests using in vivo assays indicate the chemical is not mutagenic while only in vitro bacterial assays indicated some mutagenicity concerns.

Given the preponderance of studies indicating nPB is not mutagenic, the low level of concern was warranted.

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

nPB was assigned a score of **HIGH** for reproductive toxicity based on identification by numerous sources equivalent to a high level of concern using the GreenScreen criteria. These sources the NIH National Toxicology program as a Category A 'Clear evidence of adverse reproductive effects', placement on the Cal EPA Prop 65 list as known to cause reproductive toxicity in both males and females, and identification as a Category 1B reproductive toxicant by the European Commission's Classification and Labelling Program.

These conclusions are supported by several scientific studies indicating a broad range of reproductive impacts. As the level of concern is based upon an authoritative sources and scientific studies, it is bolded in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:*
    - US NIH - National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) Reproductive & Developmental Monographs: A -Clear evidence of adverse reproductive toxicant effects (Pharos).
    - Cal/EPA Prop 65: Chemicals known to cause cancer & reproductive toxicity, female reproductive toxicity (Pharos).
    - Cal/EPA Prop 65: Chemicals known to cause cancer & reproductive toxicity, male reproductive toxicity (Pharos).
    - EC-REACH SVHCs for authorisation: Toxic to Reproduction candidate list (Pharos).
    - EC-Risk Phrases: R60, may impair fertility (Pharos).
    - EC-CLPGHS Hazard Statements: H360FD, may damage fertility (Pharos).
    - EC-CLP Inventory: Category 1B, reproductive toxicity (Pharos).

  - *Screening:*
    - EC-REACH Annex XVII (CMR) Only Toxic to Reproduction Category 2, substances which should be regarded as if they impair fertility in humans (Pharos).
    - Japan METI/MOE: GHS Classifications Category 2, toxic to reproduction (Pharos).

- *NIH Nationa*l Library of Medicine Hazardous Substances Databank

  - Results: Toxic to male rates although testicular toxicity and toxic mechanism induced by the two propyl bromide esters may be different.
    Species: Rat.
    Exposure route: Not stated although summary suggests oral.
    Method: Not stated.

Reliability: Not stated.

'The aim of this study was to investigate the different testicular toxicity and the role of apoptosis in the possible mechanism induced by the two isomers of bromopropanes (BPs) in the same dosage. Following the 14-day treatment with a single dose of 1-BP and 2-BP (1 g/kg), male rats were killed and a series of experiments were performed. 1-BP and 2-BP both significantly decreased the epididymal sperm count, while only 2-BP induced an increase in sperms with abnormal heads. Morphological evaluation showed that 1-BP did not cause morphological changes in seminiferous epithelium, but 2-BP treatment resulted in the disappearance of spermatogonia, atrophy of the seminiferous tubules and degeneration of germ cells. 2-BP significantly increased the TUNEL-positive cells and the activation of caspase-3 and decreased the genes and proteins expression of Bax, Bcl-2 and p53. In contrast, there were no significant changes in the expression of apoptosis-related genes and proteins in 1-BP group, though the TUNEL-positive cells were significantly increased. Taken together, this study indicated that those two isomers both have toxicity in male rats, however, the testicular toxicity and the role of apoptosis in the toxic mechanism induced by 1-BP and 2-BP may be different.'

- Results: NOEL = 100 ppm.
  Species: Rat.
  Exposure route: Not stated although summary suggests inhalation.
  Method: Not stated.
  Reliability: Not stated.

'*In this two-generation study, 7-week-old rats were exposed 6 hours/day, 7 days/week for 70 days prior to mating at 0, 100, 250, 500, or 750 ppm 1-BP. Females were not exposed on postnatal day 0 to 4 and only they, not their litters, were exposed during postnatal days 5 to 21. F1 rats began direct exposure at weaning. Dose-related increases in estrous cycle length at >/=250 ppm, and follicular cysts and interstitial hyperplasia of ovaries at 500 ppm were observed in F0 and F1 females. Reduced fertility and litter size was observed in the F0 and F1 generations at >/=250 ppm. The no-effect level in this study was 100 ppm 1-BP.*'

- Results: Reproductive toxicity. Changes in epididymides (testicular tube), prostate and seminal vesicles, decreased testosterone levels and reduced sperm count and motility.
  Species: Rat.
  Exposure route: Inhalation.
  Method: Not stated.
  Reliability: Not stated.

'*Repeated chronic inhalation exposure of male Sprague-Dawley rats or Wistar rats to 1-BP at concentrations of >/=500 ppm resulted in reproductive toxicity. Dose-related decreases were observed in normal sperm and sperm motility at >/=500 ppm and in sperm count at 750 ppm in both F0 and F1 males. Histopathological changes in epididymides, prostate, and seminal vesicles and decreased plasma testosterone levels were observed at 800 ppm 1-BP, while reductions in sperm count and motility were observed at >/=400 ppm.*'

- Results: Ovarian dysfunction in non-pregnant female rats.
  Species: Rat.
  Exposure route: Not stated other than 'exposed.
  Method: Not stated.
  Reliability: Not stated.

'...Forty female Wistar rats were divided into four equal groups. Each group was exposed daily to 0, 200, 400, or 800-ppm 1-bromopropane for eight hours a day. After exposure for 7 weeks, all rats in the 800-ppm group became seriously ill and were sacrificed during the 8th week. The other dose groups were exposed for 12 weeks. In the 800-ppm group, but not in the other two exposed groups, body weight was significantly less than the control at each time point from 2 to 7 weeks after the beginning of exposure. Tests of vaginal smears showed a significant increase in the number of irregular estrous cycles with extended diestrus in the 400 and 800-ppm groups. Histopathological examination of the ovary showed a significant dose-dependent reduction of the number of normal antral follicles and a decrease in the number of normal growing follicles in the 400-ppm group. No significant change was found in plasma concentrations of LH or FSH in any group compared with the control. ...Results indicate that 1-bromopropane can induce a dose-dependent ovarian dysfunction in non-pregnant female rats associated with disruption in follicular growth process.'

- Results: Impaired sexual differentiation of locomotor activity, exploratory behavior and depression.
  Species: Rat.
  Exposure route: Not stated other than 'an exposure chamber.'
  Method: Not stated.
  Reliability: Not stated.

'...The effects of prenatal exposure to 1-Bromopropane (1-BP) on sexual differentiation of rat behaviors. Pregnant rats were exposed to 1-BP (700 ppm) for 6 hr/day for 20 days in an exposure chamber during gestational days 1-20. In the open-field test, 1-BP significantly reduced locomotor activity, moving velocity and the number and the duration of staying in the center zone in female rats and abolished their sex differences. The sex difference of rearing behavior was also abolished. The duration of immobility decreased in the forced swimming test and the sex difference were disappeared. These results revealed 1-BP impaired the sexual differentiation of locomotor activity, exploratory behavior and depression.'

- Results: NOAEC = 100 ppm, LOAEC = 250 ppm; altered fertility and reduced litter size and infertility had higher concentration.
  Species: Rat.
  Exposure route: Inhalation.
  Method: Not stated.
  Reliability: Not stated.

'*...The potential adverse effects of 1-BP whole-body inhalation exposure in F0 and F1 parental rats were evaluated; reproductive capabilities were examined in the F0 and F1*

generations and neonatal survival, growth and development were evaluated in F1 and F2 offspring. In this two-generation reproductive toxicity study, groups of 25 male and female Crl:CD(SD)IGS BR rats were exposed to filtered air or 100, 250, 500, or 750 ppm [0, 503, 1,257, 2,514, 3,771 mg/cu m] 1-BP vapors (99.8% purity) for 6 hours/day, 7 days/week. ...Prior to mating, the F0 female rats exhibited increased estrous cycle length. While this effect appeared to be dose-related, statistical analysis of the data was not conducted, in part because several animals in each of the high dose groups did not cycle at all. However, the study authors considered values for the 500 and 750 ppm groups to be test agent related since they exceed the range of their historic control data for this end point (4.1-5.1 days). Reproductive performance was impaired in the higher dosage F0 groups as evidenced by significant decreases in male/female mating index in the 750 ppm group, and in the male/female fertility index in the 500 and 750 ppm groups. An increased time to coitus in the F0 500 and 750 ppm groups was not statistically significant but was considered test agent related since it exceeded historical control values. None of the females in the F0 750 ppm group became pregnant. In contrast, 1-BP treatment had no effect on gestation length or complications during delivery. However, numbers of implantation sites and pups born to F0 females were significantly reduced in the 500 ppm group. At necropsy, significant reductions in F0 absolute reproductive organ weights were observed for ovary (750 ppm), cauda epididymis (500 and 750 ppm), prostate (> or = 250 ppm, but did not decrease with increasing dose), seminal vesicles (750 ppm), and pituitary (750 ppm). Significant decreases in relative weights of these organs were only observed in the 750 ppm group for caudae epididymides and ovaries. Ovarian histologic analysis in F0 rats in the 750 ppm group revealed a significant increase in the incidence of ovaries with reduced numbers of corpora lutea and with follicular luteinized cysts. In males, a slightly increased incidence of seminiferous tubule degeneration was not considered treatment related by the study authors since lesions in 4 of 6 affected rats were of minimal severity. Also, testicular sperm counts (absolute or per gram testis) were not significantly altered by treatment. An analysis of cauda epididymal spermatozoa from F0 rats revealed significant reductions in morphologically normal sperm at > or =250 ppm. However the decrease from 99.7% normal sperm in controls to 99.3% at 250 ppm was not considered by the authors to be treatment related because this value is above historical control value of 99.0%. Cauda epididymal sperm numbers were significantly reduced at 750 ppm and the percentage of motile sperm was significantly reduced at 500 and 750 ppm. A statistically significant decrease in implantation sites and in the number of offspring at birth was seen at the 500 ppm dose in both generations. The F1 rats were evaluated for postnatal growth, development, and survival. A slight, but significant, reduction in pup viability on pnd 14-21 in the F1 500 ppm group (97.7% vs. 100% in controls) was not considered of sufficient magnitude to be treatment related, especially because postnatal survival calculated from pnd 4 to pnd 21 was not different by treatment. Therefore, the authors concluded that there were no effects on pup survival. Mean offspring weights (litter as experimental unit) were lower at the 500 ppm dose in both generations. Significant reductions in F1 litter weight gain were found in males of the 250 ppm group (pnd 21-28) and 500 ppm group (pnd 4-7, 7-14, and 21-28). A significant reduction in F1 female weight gain was only noted in the 500 ppm group on pnd 21-28. The age of balanopreputial separation was significantly increased in the F1 500 ppm group but authors attributed that effect as secondary to reduced weight gain in that group. The age at which female offspring attained of vaginal patency was not significantly different in treated

F1 offspring. 1-BP exposure in the F1 animals was initiated on pnd 22. Twenty-five rats/sex/group in control and 100-500 ppm treatment groups were selected for mating. The mating experiment was conducted as described for the F0 rats. Increased estrous cycle lengths in the 250 and 500 ppm F1 groups (4.9 and 5.1 days) were within ranges of historical controls (4.1-5.1) but were nevertheless attributed by the authors to be related to 1-BP treatment. This judgment was based on the fact that 3 and 4 animals, in the 250 and 500 ppm groups, respectively, had no complete estrous cycles (versus only 1 each in the control and 100 ppm groups). ...No significant effects were noted for F1 fertility or mating indices, days to mating, gestation length, or birthing complications. However, authors noted that non-significant and non-dose-related reductions in fertility indices in the F1 100, 250, and 500 ppm groups (68, 64, 72%, respectively) were below fertility indices of historical controls (approx 90%). Mean numbers of implantation sites were reduced in the F1 dams in the 250 and 500 ppm groups with statistical significance achieved at the higher dose level. Live litter size was significantly decreased at 500 ppm. Apparent increases in the incidence of ovarian follicular cysts and interstitial cell hyperplasia (mild) in F1 females in the 500 ppm group were not statistically significant. Absolute (but not relative) epididymis and pituitary weights were significantly reduced in the F1 500 ppm males. Lesions observed in testes were considered minimal and their incidence was not altered significantly by treatment, although there appeared to be a trend. Other male reproductive organs were histologically normal. The percentage of motile sperm was slightly, but significantly, reduced in the F1 males (from 89% in controls to 85%) at 250 ppm. The study authors did not consider this treatment-related since this value exceeds that of historic controls. However, the percentage of motile sperm was further (and significantly) reduced to 74% in the 500 ppm group. The percentages of morphologically normal sperm were significantly reduced at 500 ppm. A slight but statistically significant reduction from 99.5% normal sperm in controls to 98.9% in the 100 ppm group was not considered by the study authors to be test article related because the difference was very small, and no significant changes were seen in the 250 ppm group. F2 rats were only evaluated for postnatal growth and survival to pnd 21. Postnatal weight gain in males and females was significantly reduced in the F2 500 ppm group. Survival was unaffected. [The Expert Panel identified 100 ppm as a NOAEC in this study, and 250 ppm as a LOAEC, based on decreased prostate weight in the F0 males and increased estrous cycle length in the F1 female offspring. From the perspective of the LOAECs observed, both sexes are equally sensitive to 1-BP. Alterations in male and female reproductive outcomes at 500 ppm may contribute to the altered fertility and reduced litter size seen at this concentration, and the infertility seen at 750 ppm.]'

- ECHA, 2015.
  - Results: NOAEC = 125 ppm.
    Species: Rat.
    Exposure route: Inhalation.
    Method: Not stated.
    Reliability: Not stated.

  Groups of 10 male and 10 female rats were exposed to 1-bromopropane vapor at concentrations of 0, 62.5, 125, 250, 500, or 1,000 ppm, 6 hours plus T90 (10 minutes) per day, 5 days per week for 14 weeks. Additional clinical pathology groups of 10 male and 10 female rats were exposed to the same concentrations for 23 days. All rats survived to

the end of the study. Results of sperm count and vaginal cytology evaluations showed exposure concentration-related decreases in sperm motility and counts in male rats, reaching 28% and 37%, respectively, in the 1,000 ppm group. Female rats in all three exposure groups evaluated exhibited altered estrous cycles, spending significantly more time in extended estrus and less time in extended diestrus. Followed: OECD Guideline 413 (Subchronic Inhalation Toxicity, 90-day), 2002-2003. Reliability: Reliable without restriction - Study conducted in compliance with agreed protocols, with no or minor deviations from standard test guidelines and/or minor methodological deficiencies, which do not affect the quality of the relevant results. The study report was conclusive, done to a valid guidelines and the study was conducted under GLP conditions.

- Results: NOAEC = 125 ppm.
  Species: Rat.
  Exposure route: Inhalation.
  Method: Not stated.
  Reliability: Not stated.

Groups of 10 male and 10 female mice were exposed to 1-bromopropane vapor at concentrations of 0, 62.5, 125, 250, or 500 ppm, 6 hours plus T90 (10 minutes) per day, 5 days per week for 14 weeks. One 250 ppm male and four males and five females in the 500 ppm groups died early. Male mice in the 500 ppm group had decreased sperm counts that were 28% less than that in the chamber controls. Female mice exhibited altered estrous cycles, with females in the 500 ppm group spending significantly more time in extended diestrus and those in the 250 ppm group spending significantly more time in extended estrus compared to the chamber controls. Followed: OECD Guideline 413 (Subchronic Inhalation Toxicity, 90-day), 2002-2003. Reliability: Reliable without restriction - Study conducted in compliance with agreed protocols, with no or minor deviations from standard test guidelines and/or minor methodological deficiencies, which do not affect the quality of the relevant results. The study report was conclusive, done to a valid guidelines and the study was conducted under GLP conditions.

Data Summary:

Several authoritative sources identified nPB as a reproductive toxicant. The US NIH National Toxicology Program (NTP) identified nPB as a Category A reproductive toxicant with clear evidence of adverse reproductive toxicant effects. The California EPA Prop 65 list identified nPB as known to cause reproductive toxicity in both females and males. The European Commission identified nPB as a Category 1B reproductive toxicant and assigned an R60 Risk Phrase and an H360FD Hazard Statement. It also placed nPB on its REACH list of substances of very high concern due to its reproductive toxicity. All of these sources equate to a high level of concern using the GreenScreen criteria.

Two authoritative screening lists identified a lower level of concern. The European Commission REACH Annex XVII identified nPB as a Category 2 toxicant, substances that should be regarded as if they impair fertility. This determination agrees with the Japan METI/MOE

identifying nPB as a Category 2 reproductive toxicant. These sources, however, are supplanted by determinations from the previously described authoritative bodies.

Several research studies were also identified. One study reported in the NIH's Hazardous Substances Databank (HSDB) evaluated impacts from nPB and the surrogate, 2-propyl bromide. Based upon this study, both isomers were found to be reproductive toxicants although the surrogate appeared more toxic than nPB. Two further studies in the HSDB reported an NOEL = 100 ppm and a NOAEL = 100 and LOAEC = 250 ppm, respectively. Using GHS criteria, these equate to a moderate level of concern.

Three additional studies identified nPB as an environmental toxicant with impacts to sexual differentiation, ovarian dysfunction, changes in the male reproductive system, decreased testosterone levels and reduced sperm count and motility, among others. Two inhalation studies reported by the European Chemicals Agency (ECHA), identified inhalation NOAECs = 125 ppm using OECD guidelines. Using GHS criteria, this equates to a moderate level of concern.

Using the GreenScreen criteria, a high level of concern was assigned based upon several authoritative sources including the NTP, California Prop 65, and the European Commission and several reproductive studies identifying nPB as a reproductive toxicant.

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

nPB was assigned a score of **HIGH** for developmental toxicity based on identification by the NIH's National Toxicology Program as an developmental toxicant with 'clear evidence of adverse developmental toxicant effects' and its presence on the California EPA's Prop 65 list. As these sources are authoritative, the high level of concern is bolded in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:*
    - US NIH National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR), Reproductive & Developmental Monographs: Clear evidence of adverse developmental toxicant effects (Pharos).
    - California EPA Prop 65: chemicals known to cause developmental toxicity.
    - EC-CLP: Risk Phrases: R63, possible risk to the unborn child (Pharos).
  - *Screening:* None

- NIH National Library of Medicine Hazardous Substances Databank
  - Results: NOEL = 100 ppm. Significant impacts to bone development. Decreased fetal weights observed at NOEL concentration.
    Species: Rat.
    Exposure route: Inhalation.
    Method: Not stated other than 'exposed.'
    Reliability: Not stated.

'*Pregnant Sprague-Dawley rats were exposed 6 hours/day from gestational days 6 to 19 at 0, 100, 498, or 996 ppm 1-BP, and fetuses were removed at gestational day 20. Maternal weight gain and food intake decreased at 498 ppm. Decreased fetal weight was observed at all doses. Embryotoxicity was not observed. A dose-related decrease in ossification in the litters was observed at 498 ppm, with a significant increase in bent ribs at 996 ppm. The no-observed effect level (NOEL) for maternal toxicity was 100 ppm, but decreased fetal weights were observed at this dose.*'

Data Summary:

The NIH National Toxicology Program identified nPB as a developmental toxicant with 'clear evidence of adverse developmental toxicant effects'. The California EPA also placed nPB as a developmental toxicant on their Prop 65 list. These equate to a high level of concern using GreenScreen criteria.

The European Commission assigned nPB a risk phrase of R63 which equates to a moderate level of concern using the GreenScreen criteria. An inhalation study in NIH's Hazardous Substances Databank (HSDB) reported an NOEL = 100 ppm which moderate level of concern.

nPB was assigned a score of high for developmental toxicity based upon the assessment of nPB as a developmental toxicant by the National Toxicology Program and the California EPA.

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

nPB was assigned a score of DATA GAP for endocrine activity based on no data identified for this hazard endpoint.

- Authoritative and Screening Lists
  - *Authoritative:* None
  - *Screening:* None

- Source
  - Data: None

Data Summary:

nPB was assigned a score of data gap for endocrine activity based on inability to find any data evaluating the chemical or the identified analog for endocrine activity.

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 (the asterisk indicates repeated exposure). For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints. When classifying hazard for Systemic Toxicity/Organ Effects and Neurotoxicity endpoints, repeated exposure results are required and preferred. Lacking repeated*

exposure results in a data gap. Lacking single exposure data does not result in a data gap when repeated exposure data are present (shade out the cell in the hazard table and make a note). If data are available for both single and repeated exposures, the more conservative value is used.

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

nPB was assigned a score of **MODERATE** for acute mammalian toxicity based on the European Union's assigning an Risk Phrase of R20 (high to moderate level of concern in the GreenScreen criteria) and numerous studies indicating a moderate or low level of concern. The scientific studies indicate the moderate level of concern for acute mammalian toxicity is appropriate for nPB.

As the level of concern is based upon authoritative sources and scientific studies, it is bolded in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:*
    - EC - Risk Phrases - R20: Harmful by inhalation. (Pharos)
  - *Screening:* None

- NIH National Library of Medicine Hazardous Substances Databank, 2015.
  - Results: No deaths or treatment-related effects.
    Species: Rat.
    Exposure route: Dermal.
    Method: Not stated.
    Reliability: Not stated.

    '*The dermal toxicity of 1-BP was investigated in Sprague-Dawley rats at a dose of 2,000 mg/kg covered by a semi-occlusive dressing for 24 hours. There was no cutaneous reaction to 1-BP and there were no deaths or treatment-related effects.*'

  - Results: LC_{50}= 6,958.
    Species: Rat.
    Exposure route: Inhalation, 4 hours.
    Method: Not stated.
    Reliability: Not stated.

    An acute inhalation toxicity study of 1-BP was conducted using 7-9 week old male and female Wistar rats ... . In a limit test, 5 rats/sex/group were exposed to 0 or 34.6 g/cu m [34, 600 mg/cu m, equivalent to 6,879 ppm]. In the main part of the study, 5 males and 5 females/group were exposed to 0, 30.2, 35.1, 37.0, or 42.5 g/cu m [30,200, 35,100, 37,000, or 42,500 mg/cu m, equivalent to 6,003, 6,997, 7,355 and 8,448 ppm, respectively] 1-BP (99.5%). Five satellite males/group were exposed to 0 or 36.4 g/cu m [36,400 mg/cu m, equivalent to 7,237 ppm] and blood was collected 24 hours and 13 days after exposure for hematology. All exposures were conducted for 4 hours in a nose-only chamber (flow-past

system). ...Lungs and testes from control animals and those exposed to 34.6 (males only) and 42.5 g/cu m were weighed and examined microscopically (tissue fixed in 10% formalin). All animals exposed to 37.0 and 42.5 g/cu m died on test. Most animals exposed to 35.1 g/cu m died (7/10) and some animals exposed to 34.6 g/cu m died (3/10). The LC_{50} was estimated at 35.0 g/cu m [6,958 ppm]. Clinical signs included respiratory distress and general weakness. Surviving animals gained weight over the 14 days. There was an increase in leukocyte count, hemoglobin, and packed cell volume on day 2 for the 36.4 g/cu m group [no statistical evaluation], but these differences resolved by day 14. There was no apparent change in relative testis weight and no microscopic testicular lesions in animals exposed to 1-BP. Pulmonary lesions consisting of edema and emphysema were observed in the 1-BP-exposed animals. The Expert Panel selected a NOEC of 30.2 g/cu m.'

- LC_{50} = 7,000 ppm/4 hr; Rat (Wister), inhalation.
- LC_{50} = 14,374 ppm/4hr; Rat (Sprague-Dawley), inhalation.
- LD_{50} > 2,000 mg/kg; Rat, oral.
- LD_{50} > 2,000 mg/kg; Rat (Sprague-Dawley), dermal.

- European Chemicals Agency (ECHA), 2015.
  - Results: LD_{50} = 540 mg/kg bw.
    Species: Rabbit.
    Exposure route: Oral.
    Method: Not stated.
    Reliability: Reliable with restrictions - Study conducted in accordance with generally accepted scientific principles, possibly with incomplete reporting or methodological deficiencies, which do not affect the quality of the relevant results.

  - Results: LD_{50} = 4,260 mg/kg bw.
    Species: Rat.
    Exposure route: Oral.
    Method: Not stated.
    Reliability: Reliable with restrictions - Study conducted in accordance with generally accepted scientific principles, possibly with incomplete reporting or methodological deficiencies, which do not affect the quality of the relevant results.

An acute oral study was performed on young adult male Charles River rats at doses of 0.63, 0.8, 1.25, 2, 3.14, 5 and 6.3 ml/kg bw. The acute oral LD_{50} to male rats of 1-bromopropane was determined as 3.16 ml/kg bw with 95% confidence limits of 1.62 - 6.17 ml/kg bw. This is equivalent to 4,260 mg/kg.

  - Results: LC_{50} = 25 to 35 mg/L.
    Species: Rat.
    Exposure route: Inhalation.
    Method: Not stated.
    Reliability: Reliable with restrictions - Study conducted in accordance with generally accepted scientific principles, possibly with incomplete reporting or methodological deficiencies, which do not affect the quality of the relevant results.

In an acute inhalation study, 7 week old male and female Sprague Dawley rats were exposed to 1-bromopropane for 6 hours at nominal concentrations of 25, 35, 50 and 100 mg/L. The 6 hour LC_{50} of 1-bromopropane was found to be between 25 and 35 mg/L.

- Registry of Toxic Effects of Chemical Substances (RTECS), 2015.
  - Results: LD_{50} = 4,700 mg/kg, details of toxic effects not reported other than lethal dose value.
    Species: Mouse.
    Exposure route: Oral.
    Method: Not stated.
    Reliability: Not stated.

  - Results: LD_{50} = 3,600 mg/kg, details of toxic effects not reported other than lethal dose value.
    Species: Rat.
    Exposure route: Oral.
    Method: Not stated.
    Reliability: Not stated.

  - Results: LC_{50} = 7,100 mg/m^3, details of toxic effects not reported other than lethal dose value.
    Species: Mouse.
    Exposure route: Inhalation.
    Method: Not stated.
    Reliability: Not stated.

  - Results: LC_{50} = 19,700 mg/m^3, details of toxic effects not reported other than lethal dose value.
    Species: Rat.
    Exposure route: Inhalation.
    Method: Not stated.
    Reliability: Not stated.

Data Summary:

The European Commission assigned nPB an R20 risk phrase indicating harm by inhalation. R20 equates to either a high or moderate level of concern in the GreenScreen criteria. The NIH's Hazardous Substances Database (HSDB) reported several inhalation studies with LC_{50} (ranging from 6,958 to 14,374 ppm) and LD_{50} (> 2,000 ppm) values. The LC_{50} and LD_{50} values equate to a low level of concern in the GreenScreen criteria. Several other studies were identified where no lethal values could be calculated based upon few toxicological impacts.

The European Chemicals Agency identified three acute toxicity studies. Two oral studies reported LC_{50} values of 540 (moderate level of concern) and 4,260 mg/kg bw (low level of

concern) for rabbits and rats, respectively. An acute inhalation study reported LC_{50} values ranging from 25-35 mg/L (low level of concern).

The Registry of Toxic Effects of Chemical Substances (RTECs) reports four studies, two oral and two inhalation. The two oral studies reported LD_{50} values of 3,600 and 4,700 ppm, both of which equate to a low level of concern in the GreenScreen criteria. The two inhalation studies reported LC_{50} values of 7,100 and 19,700 mg/m^3. These values convert to 7.1 and 19.7 mg/L, respectively and equate to a high or moderate level of concern in the GreenScreen criteria, respectively.

Acute toxicity values for nPB varied widely. Values ranged from high and moderate for inhalation studies reported in RTECs and numerous studies showing low levels of concern.

As the R20 risk phrase equates to either a high or moderate level of inhalation concern using GreenScreen criteria and inhalation studies support a moderate level of concern, nPB was assigned a moderate level of concern as an average of the widespread analytical results.

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)

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

nPB was assigned a score of MODERATE for single-dose systemic toxicity/organ effects based on both the European Commission's and the European Chemicals Agency (ECHA) identification of the risk phrase R37 and ECHA's assignment of a hazard phrase of H335. As these are authoritative sources, the moderate level of concern is bolded in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:*
    - EC - Risk Phrases - R37: Irritating to respiratory system. (Pharos)

Screening: None

- ECHA, 2015.
  - H335: May cause respiratory irritation
  - R36/37/38 – Irritating to eyes, respiratory system and skin

- NIH National Library of Medicine Hazardous Substances Databank, 2015.
  - Result: LC_{50} = 14,374 ppm (72.3 mg/L), NOEC = 11,000 ppm (55.3 mg/L.
    Species: Rat.
    Exposure route: Inhalation, 4 hours.
    Method: Not stated.
    Reliability: Not stated.

  'The acute ... inhalation toxicity of 1-bromopropane (1-BP) in 11-week-old male and female Sprague-Dawley rats. ...Rats inhaled reagent grade 1-BP... . ...5 rats/sex/group inhaled 0, 11,000, 13,000 15,000, or 17,000 ppm [55,337, 65,398, 75,460, or 85,521 mg/cu m] 1-BP for

4 hours. Rats were observed for 2 weeks following exposure. Clinical signs of toxicity in treated groups during exposure included piloerection, reduced activity, ataxia, lacrimation, and reduced response to noise. Death was observed within 24 hours of exposure in groups exposed to 13,000 ppm and higher; incidence of death was dose-related and reached 100% in the highest dose. All surviving rats clinically recovered 24 hours after the exposure period. An LC_{50} of 14,374 ppm (95% confidence limit: 13,624-15,596 ppm) was calculated. The lowest lethal concentration was <11,833 ppm and the LC_{100} was >18,186 ppm. At the end of the observation period, all surviving rats were sacrificed by carbon dioxide and necropsied; abnormal tissues were examined histologically. Cytoplasmic vacuolation of hepatocytes surrounding the central vein was observed in an unspecified number of treated rats but the effect was not dose-dependent. The Expert Panel selected a NOEC of 11,000 ppm.'

Data Summary:

The European Chemicals Agency (ECHA) assigned nPB a risk phrase of R37, irritating to the respiratory system and a hazard phrase of H335. These equate to a moderate level of concern using the GreenScreen criteria. One inhalation study was identified that produced an LC50 of 72.3 mg/L. This is outside the ranges used in the GreenScreen and suggests a moderate or low level of concern.

Based upon this data, nPB was assigned a moderate level of concern.

(ST-repeat) Group II* Score (repeat dose: vH, H, M or L): *M*

nPB was assigned a score of **MODERATE** for repeated-dose systemic toxicity/organ effects based on the European Commission's assigned a hazard phrase of H373 due to damage to the liver indicating a moderate level of concern. Although this is an authoritative source, all study data suggested a low level of concern; therefore, as there is a conflict between the European's Commission's hazard phrase and all identified scientific data, the moderate is italicized in the GreenScreen Hazard Summary Table to indicate some uncertainty with this hazard endpoint.

- Authoritative and Screening Lists
  - *Authoritative:*
    - EC - CLP/GHS Hazard Statements - H373 May cause damage to organs through prolonged or repeated exposure (Pharos)

  - *Screening:* None

- European Chemicals Agency (ECHA), 2015.
  - Results: NOAEC = 250 ppm, mild hepatotoxicity, cytoplasic vacuolization of liver.
    Species: Rat.
    Exposure route: Inhalation, 6 hours plus 10 minutes, 5 days/week for 14 weeks.
    Method: OECD Guideline 413 (Subchronic Inhalation Toxicity, 90-day), 2002-2003.
    Reliability: Reliable without restriction - Study conducted in compliance with agreed protocols, with no or minor deviations from standard test guidelines and/or minor methodological deficiencies, which do not affect the quality of the relevant results. The

study report was conclusive, done to a valid guidelines and the study was conducted under GLP conditions.

'*Groups of 10 male and 10 female rats were exposed to 1-bromopropane vapor at concentrations of 0, 62.5, 125, 250, 500, or 1,000 ppm, 6 hours plus T90 (10 minutes) per day, 5 days per week for 14 weeks. Additional clinical pathology groups of 10 male and 10 female rats were exposed to the same concentrations for 23 days. All rats survived to the end of the study. Mean body weights of 1,000 ppm males were significantly less than those of the chamber controls. The increases in sorbitol dehydrogenase activities in 500 ppm males and 1,000 ppm males and females were consistent with the histopathologic evidence of mild hepatotoxicity caused by 1-bromopropane. Liver weights of males exposed to 250 ppm or greater and of females exposed to 125 ppm or greater were significantly increased. Spleen and kidney weights of 1,000 ppm females were significantly increased. The incidences of cytoplasmic vacuolization of the liver were significantly increased in males exposed to 250 ppm or greater and in females exposed to 500 ppm or greater. Hepatocyte degeneration was also observed in 1,000 ppm females.*

- Results: NOAEC = 125 ppm, non-neoplastic lesions in nose, larynx, trachea, lung and liver (males) and adrenal cortex (females).
  Species: Mice.
  Exposure route: Inhalation, 6 hours plus 10 minutes, 5 days/week for 14 weeks.
  Method: OECD Guideline 413 (Subchronic Inhalation Toxicity, 90-day), 2002-2003.
  Reliability: Reliable without restriction - Study conducted in compliance with agreed protocols, with no or minor deviations from standard test guidelines and/or minor methodological deficiencies, which do not affect the quality of the relevant results. The study report was conclusive, done to a valid guidelines and the study was conducted under GLP conditions.'

'*Groups of 10 male and 10 female mice were exposed to 1-bromopropane vapor at concentrations of 0, 62.5, 125, 250, or 500 ppm, 6 hours plus T90 (10 minutes) per day, 5 days per week for 14 weeks. One 250 ppm male and four males and five females in the 500 ppm groups died early. Mean body weights of exposed groups were similar to those of the chamber controls. Lethargy was observed in males and females exposed to 500 ppm, and abnormal breathing was observed in moribund mice. The kidney, liver, and lung weights of 500 ppm females were significantly greater than those of the chamber controls. The kidney weights of 500 ppm males were significantly decreased. Non-neoplastic lesions were observed in the nose, larynx, trachea, lung, and liver of 500 ppm males and females and in the adrenal cortex of 500 ppm females.*

- Results: NOAEC < 125 ppm, microscopic lesions in the lung, liver and nose.
  Species: Mice.
  Exposure route: Inhalation, 6 hours plus 12 minutes, 5 days/week for 14 weeks.
  Method: OECD Guideline 413 (Subchronic Inhalation Toxicity, 90-day), 2002.
  Reliability: Reliable without restriction - Study conducted in compliance with agreed protocols, with no or minor deviations from standard test guidelines and/or minor methodological deficiencies, which do not affect the quality of the relevant results. The

study report was conclusive, done to a valid guidelines and the study was conducted under GLP conditions.'

'*Groups of five male and five female mice were exposed to 1-bromopropane vapor at concentrations of 0, 125, 250, 500, 1,000, or 2,000 ppm, 6 hours plus T90 (12 minutes) per day, 5 days per week for 17 days. All 2,000 ppm males, two 2,000 ppm females, four 500 ppm males, one 1,000 ppm male, and one 1,000 ppm female died early. The mean body weight gain of 1,000 ppm males was significantly less than that of the chamber controls. Abnormal breathing, lethargy, and eye discharge were observed primarily during week 1 in groups exposed to 500 ppm or greater. Liver weights of 1,000 ppm males and of females exposed to 500 ppm or greater were significantly increased. Kidney weights of 1,000 and 2,000 ppm females were significantly increased. Microscopic lesions related to 1-bromopropane exposure occurred in the lung, liver, and nose of males and females and were primarily seen in mice exposed to 500 ppm or greater.*

- Results: NOAEC = 250 ppm, nasal lesions, respiratory epithelial necrosis and respiratory epithelial regeneration.
  Species: Rat.
  Exposure route: Inhalation, 6 hours plus 12 minutes, 5 days/week for 16 days.
  Method: OECD Guideline 412 (Repeat Dose Inhalation Toxicity, 28/14-day), 2002.
  Reliability: Reliable without restriction - Study conducted in compliance with agreed protocols, with no or minor deviations from standard test guidelines and/or minor methodological deficiencies, which do not affect the quality of the relevant results. The study report was conclusive, done to a valid guidelines and the study was conducted under GLP conditions.

'*Groups of five male and five female rats were exposed to 1-bromopropane vapor at concentrations of 0, 125, 250, 500, 1,000, or 2,000 ppm, 6 hours plus T90 (12 minutes) per day, 5 days per week for 16 days. All rats survived to the end of the study except one 500 ppm male. Mean body weights of 2,000 ppm rats were significantly less than those of the chamber controls. The absolute kidney weight of 1,000 ppm males, relative kidney weights of all exposed groups of males, and absolute and relative kidney weights of all exposed groups of females were significantly increased. The absolute and relative liver weights of 1,000 ppm males, relative liver weights of 500 and 2,000 ppm males, and absolute and relative liver weights of 500 ppm or greater females were significantly increased. Nasal lesions included suppurative inflammation in males exposed to 500 ppm or greater, respiratory epithelial necrosis in 1,000 and 2,000 ppm males, and respiratory epithelial regeneration in 1,000 and 2,000 ppm females.*

- NIH National Library of Medicine Hazardous Substances Databank, 2015.
  - Results: Few impacts found. No LC_{50} or NOEC determined.
    Species: Rat.
    Exposure route: Inhalation, 6 hours/day, 5 days/week for 8 weeks.
    Method: Not stated.
    Reliability: Not stated.

'Subchronic or Prechronic Exposure/ Sprague-Dawley rats exposed 6 hours/day, 5 days/week for 8 weeks at 0, 50, 300, or 1800 ppm 1-BP showed decreased body weights and increased liver weights at the highest concentration. No other significant changes in food consumption, urinalysis, hematology, or serum biochemistry were observed. All treated rats showed signs of cytoplasmic vacuolization in centrilobular hepatocytes, but these lesions did not exhibit a dose-dependence. Histopathological examinations did not reveal any treatment-related effects in other tissues.'

- Results: Few impacts found. No LC_{50} determined. NOEC = 200 ppm.
  Species: Rat.
  Exposure route: Inhalation, 6 hours/day, 5 days/week for 13 weeks.
  Method: Not stated.
  Reliability: Not stated.

'Subchronic or Prechronic Exposure/ Sprague-Dawley rats were exposed 6 hours/day, 5 days/week for 13 weeks at 100, 200, 400, or 600 ppm. No clinical signs related to treatment were observed. Histopathology revealed centrilobular vacuolization of the liver in the two highest dose groups. No other treatment-related effects were observed. The no-effect level for the liver effects was 200 ppm'.

Data Summary:

The European Commission assigned nPB a hazard statement of H373, may cause damage to the liver through prolonged or repeated exposure. This equates to a moderate level of concern in the GreenScreen criteria.

The European Chemicals Agency (ECHA) reported four studies with NOAEC values ranging from < 125 to 250 ppm, equivalent to a low level of concern. Two studies listed in the NIH's Hazardous Substances Databank were unable to identify any concerns which equate to a low level of concern.

Although several scientific studies indicated a low level of concern, nPB was assigned a conservative score of moderate for systemic toxicity/organ effects based on the authoritative European Commission's hazard statement of H373.

Neurotoxicity (N)

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

nPB was assigned a score of **MODERATE** for single dose neurotoxicity based on the assignment of the Hazard Statement H336 by an authoritative source, the European Chemicals Agency. nPB was identified as causing drowsiness or dizziness although the affected organs were not identified.

As H336 can either be a moderate or low level of concern and no additional data could be identified to better clarify the level of concern, the more conservative moderate level of concern

was selected. Since the moderate level of concern is based upon incomplete information, it is italicized in the GreenScreen Hazard Table for nPB.

- Authoritative and Screening Lists
  - *Authoritative:*
    - EC -CLP/GHS Hazard Statements – STOT Single Exp. 3 H336: May cause drowsiness or dizziness. Affected organs: not specified. (ECHA, 2015)
  - *Screening:* None

Data Summary:

Data on single dose neurotoxicity is limited. The European Chemicals Agency (ECHA) identified a Hazard Statement of H336 although the affected organs were not identified. This translates into a range of concern from low to moderate in the GreenScreen criteria.

Based upon this limited information, nPB was assigned a score moderate for single dose neurotoxicity based upon a Hazard Statement from an authoritative source, ECHA but without additional data to better clarify the exact level of concern.

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

nPB was assigned a score of **MODERATE** for repeated dose neurotoxicity based on the European Commission's assigning a Hazard Phrase of H373 and scientific studies which document negative impacts to the central nervous system. Since the moderate level of concern was based upon an authoritative source and scientific studies, it is bolded in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:*
    - EC - CLP/GHS Hazard Statements: STOT Rep. Exp. 2 H373: May cause damage to organs through prolonged or repeated exposure. Affected Organs: Liver and Central Nervous System. (ECHA, 2015)

  - *Screening:* None

- NIH National Library of Medicine Hazardous Substances Databank, 2015.
  - Results: Impacts found at lowest conc. tested (400 ppm). No LC_{50} or NOEC determined although histopathological lesions were found in the Central Nervous System (CNS) at 400 ppm (2.0 mg/L).
    Species: Rat.
    Exposure route: Inhalation, 6 hours/day, 5 days/week for 28 days.
    Method: Not stated.
    Reliability: Not stated.

  'Subchronic or Prechronic Exposure/ Whole-body inhalation exposure of Sprague-Dawley rats 6 hours/day, 5 days/week over 28 days to 1-BP vapors at 0, 400, 1,000, or 1,600 ppm

produced significant mortality (8/10) at the highest concentration. Significant effects were observed in rats exposed to 1,000 and 1,600 ppm including clinical signs of deteriorating condition, abnormal gait and decreased body weights and food consumption. Other effects included changes in erythrocyte and blood chemistry parameters, increases in liver and kidney weights, and decreases in brain weight. Histopathological lesions were observed in the central nervous system (CNS), urinary system, nasal cavities, sternal bone marrow, lymphoid tissues, and male reproductive system. Exposure at 400 ppm produced histopathological lesions in the CNS. Thus, a no-effect level could not be identified in this study.'

- Results: Significant changes in amino acid contents of rat brains. Results found at 50 ppm (0.25 mg/L), the lowest dose tested.
  Species: Rat.
  Exposure route: Inhalation, 8 hours, 7 days/week for 21 days.
  Method: Not stated.
  Reliability: Not stated.

'*The present study investigated the effects of 1-bromopropane (1BP) on brain neuro-active substances of rats to determine the extent of its toxicity to the central nervous system (CNS). The authors measured the changes in neurotransmitters (acetylcholine, catecholamine, serotonin and amino acids) and their metabolites or precursors in eight brain regions after inhalation exposure to 1BP at 50 to 1,000 ppm for 8 hr per day for 7 days per week for 3 weeks. Rats were sacrificed at 2 hr (Case 1), or at 19 hr (Case 2) after the end of exposure. In Case 1, the level of 5-hydroxyindoleacetic acid (5HIAA) was lowered in some brain regions by 1BP exposure. The decrease of 5HIAA in the frontal cortex was statistically significant at 50 ppm 1BP exposure. In Case 2, gamma-amino butyric acid (GABA) and taurine were decreased in many brain regions of exposed rats, and a significant decrease of taurine in the midbrain occurred at 50 ppm 1BP exposure. In both cases of 2 hr and 19 hr intervals from the end of exposure to sacrifice, aspartate and glutamine levels were elevated in many brain regions, but the acetylcholine level did not change in any brain region. Three-week repeated exposure to 1BP produced significantly changes in amino acid contents of rat brains, particularly at 1,000 ppm.*'

- Results: Degeneration of noradrenergic axons in the brain. No data provided on lowest effect levels.
  Species: Rat.
  Exposure route: Inhalation, no other data provided.
  Method: Not stated.
  Reliability: Not stated.

'*1-Bromopropane (1-BP) has been used as an alternative to ozone-depleting solvents. Previous studies showed that 1-BP is neurotoxic in animals and humans. In humans, exposure to 1-BP caused various neurological and neurobehavioral symptoms or signs including depressive or irritated mood. However, the neurobiological changes underlying the depressive symptoms induced by 1-BP remain to be determined. The depressive symptoms are thought to be associated with degeneration of axons containing noradrenaline and serotonin. Based on this hypothesis, the present study examined the effects of repeated*

exposure to 1-BP on serotonergic and noradrenergic axons. Exposure to 1-BP induced dose-dependent decreases in the density of noradrenergic axons in the rat prefrontal cortex, but no apparent change in the density of serotonergic axons. The results suggest that depressive symptoms in workers exposed to 1-BP are due, at least in part, to the degeneration of noradrenergic axons in the brain.'

- Results: Oxidative damage of cellular proteins, decreased triosephosphate isomerase (TPI) activity and elevated advanced glycation end-product (AGE) levels. Elevated AGE levels can lead to increased neurodegenerative diseases (Oleniuc, 2011) and chronic developmental diseases such as Alzheimer's disease (Luevano-Contrareras, 2010). No data available on lowest effect levels.
  Species: Rat.
  Exposure route: Inhalation, 8 hr/day for 1 or 4 weeks.
  Method: Not stated.
  Reliability: Not stated.

'*1-Bromopropane (1-BP) is neurotoxic in both experimental animals and humans. Previous proteomic analysis of rat hippocampus implicated alteration of protein expression in oxidative stress, suggesting that oxidative stress plays a role in 1-BP-induced neurotoxicity. To understand this role at the protein level, the authors exposed male F344 rats to 1-BP at 0, 400, or 1000 ppm for 8hr/day for 1 week or 4 weeks by inhalation and quantitated changes in hippocampal protein carbonyl using a protein carbonyl assay, two-dimensional gel electrophoresis (2-DE), immunoblotting, and matrix-assisted laser-desorption ionization time-of-flight mass spectrometry (MALDI-TOF-TOF/MS). Hippocampal reactive oxygen species and protein carbonyl were significantly increased, demonstrating 1-BP-associated induction of oxidative stress and protein damage. MALDI-TOF-TOF/MS identified 10 individual proteins with increased carbonyl modification ($p < 0.05$; fold-change >/= 1.5). The identified proteins were involved in diverse biological processes including glycolysis, ATP production, tyrosine catabolism, GTP binding, guanine degradation, and neuronal metabolism of dopamine. Hippocampal triosephosphate isomerase (TPI) activity was significantly reduced and negatively correlated with TPI carbonylation ($p < 0.001$; $r = 0.83$). Advanced glycation end-product (AGE) levels were significantly elevated both in the hippocampus and plasma, and hippocampal AGEs correlated negatively with TPI activity ($p < 0.001$; $r = 0.71$). In conclusion, 1-BP-induced neurotoxicity in the rat hippocampus seems to involve oxidative damage of cellular proteins, decreased TPI activity, and elevated AGEs.*'

- Results: Morphological change in the microglia and oxidative stress. No data provided on lowest effect levels.
  Species: Rat.
  Exposure route: No information provided other than 'exposed', 8 hr/day for 4 weeks.
  Method: Not stated.
  Reliability: Not stated.

'*…1-BP, an alternative to ozone-depleting solvents, is reported to exhibit neurotoxicity and reproductive toxicity in animals and humans. However, the underlying mechanism of the toxicity remains elusive. This study was designed to identify the microglial changes and*

oxidative stress in the central nervous system (CNS) after 1-BP exposure. Four groups of Wistar-ST rats (n=12 each) were exposed to 0, 400, 800 and 1000 ppm of 1-BP, 8hr/day for 28 consecutive days. The cerebellum was dissected out in 9 rats of each group and subjected to biochemical analysis, while the brains of the remaining 3 rats were examined immunohistochemically. Exposure to 1-BP increased the levels of oxidative stress markers (thiobarbituric acid reactive substances (TBARS), protein carbonyl and reactive oxygen species (ROS)) in a dose-dependent manner. Likewise, there was also 1-BP dose-dependent increase in nitric oxide (NO) and dose-dependent decrease in protein concentrations in the cerebellum. Immunohistochemical studies showed 1-BP-induced increase in cd11b/c-positive microglia area in the white matter of the cerebellar hemispheres. The results showed that exposure to 1-BP induced morphological change in the microglia and oxidative stress, suggesting that these effects are part of the underlying neurotoxic mechanism of 1-BP in the CNS.'

- Results: Degeneration of cerebellum, adverse effects on myelination. Results shown at lowest level tested, 400 ppm, which suggests NOAEL < 400 ppm (2.01 mg/L). This study was conducted only over a 28 day exposure period which is less than the standard 90 day period recommended by approved methodologies. The results should be adjusted accordingly.
  Species: Rat.
  Exposure route: No information provided other than 'exposed', 8 hr/day, 7 days a week for 4 weeks.
  Method: Not stated.
  Reliability: Not stated.

'*Human cases of 1-bromopropane (1-BP) toxicity showed ataxic gait and cognitive dysfunction, whereas rat studies showed pyknotic shrinkage in cerebellar Purkinje cells and electrophysiological changes in the hippocampus. The present study investigated the effects of 1-BP on astrocytes and oligodendrocytes in the rat cerebellum and hippocampus to find sensitive markers of central nervous system toxicity. Forty-eight F344 rats were divided into four equal groups and exposed to 1-BP at 0, 400, 800 and 1,000 ppm for 8 hr/day, 7 days/week for 4 weeks. Nine and three rats per group were used for biochemical and histopathological studies, respectively. Kluver-Barrera staining showed pyknotic shrinkage in the cytoplasm of Purkinje cells and nuclei of granular cells in the cerebellum at 1,000 ppm. Immunohistochemical analysis showed increased length of glial fibrillary acidic protein (GFAP)-positive processes of astrocytes in the cerebellum, hippocampus and dentate gyrus at 800 and 1,000 ppm. The myelin basic protein (MBP) level was lower at 1,000 ppm. The numbers of astrocytes and granular cells per tissue volume increased at 400 ppm or higher. The present study showed that elongation of processes of astrocytes accompanies degeneration of granular cells and Purkinje cells in the cerebellum of the rats exposed to 1-BP. The decrease in MBP and number of oligodendrocytes suggest adverse effects on myelination. The increase in astrocyte population per tissue volume in the cerebellum might be a sensitive marker of 1-BP neurotoxicity, but the underlying mechanism for this change remains elusive.*'

- Results: Reduced neurogenesis with impacts to hippocampus, prefrontal cortex and striatum. Results observed at 800 ppm (4.02 mg/L) and no reported impacts at 400 ppm (2.01 mg/L); therefore, the NOAEL is between 400 to 800 ppm (2.01 to 4.02 mg/L).
  Species: Rat.
  Exposure route: No information provided other than 'exposed' although inhalation likely, 8 hr/day for 1, 2 and 4 weeks.
  Method: Not stated.
  Reliability: Not stated.

'*1-Bromopropane (1-BP) intoxication is associated with depression and cognitive and memory deficits. The present study tested the hypothesis that 1-BP suppresses neurogenesis in the dentate gyrus, which is involved in higher cerebral function, in adult rats. Four groups of 12 male Wistar rats were exposed to 0, 400, 800, 1000 ppm 1-BP, 8 h/day for 7 days. Another four groups of six rats each were exposed to 0, 400, 800 and 1000 ppm 1-BP for 2 weeks followed by 0, 200, 400 and 800 ppm for another 2 weeks, respectively. Another four groups of six rats each were exposed to 0, 200, 400 and 800 ppm 1-BP for 4 weeks. Rats were injected with 5-bromo-2'-deoxy-uridine (BrdU) after 4-week exposure at 1000/800 ppm to examine neurogenesis in the dentate gyrus by immunostaining. We measured factors known to affect neurogenesis, including monoamine levels, and mRNA expression levels of brain-derived neurotrophic factor (BDNF) and glucocorticoid receptor (GR), in different brain regions. BrdU-positive cells were significantly lower in the 800/1000 ppm-4-week group than the control. 1-Week exposure to 1-BP at 800 and 1000 ppm significantly reduced noradrenalin level in the striatum. Four-week exposure at 800 ppm significantly decreased noradrenalin levels in the hippocampus, prefrontal cortex and striatum. 1-BP also reduced hippocampal BDNF and GR mRNA levels. Long-term exposure to 1-BP decreased neurogenesis in the dentate gyrus. Downregulation of BDNF and GR mRNA expression and low hippocampal norepinephrine levels might contribute, at least in part, to the reduced neurogenesis.*'

- Results: Cognitive dysfunction, enhanced lipid peroxidation of brain, CNS damage. No data provided on lowest effect levels.
  Species: Rat.
  Exposure route: No information provided other than 'treated' although oral likely, 12 days.
  Method: Not stated.
  Reliability: Not stated.

'*1-Bromopropane (1-BP), an alternative to ozone-depleting solvents (ODS), exhibits central nervous system (CNS) toxicity in animals and humans. This study was designed to relate CNS damage by Morris water maze (MWM) test and oxidative stress to 1-BP exposure in the rat. Male Wistar rats were randomly divided into 4 groups (n=10), and treated with 0, 200, 400 and 800 mg/kgbw 1-BP for consecutive 12 days, respectively. From day 8 to day 12 of the experiment, MWM test was employed to assess the cognitive function of rats. The cerebral cortex of rats was obtained immediately following the 24hr after MWM test conclusion. Glutathione (GSH), oxidized glutathione (GSSG) and total thiol (total-SH) content, GSH reductase (GR) and GSH peroxidase (GSH-Px) activities, malondialdehyde (MDA) level, as*

well as 4-hydroxynonenal (4-HNE) and MDA modified proteins in homogenates of cerebral cortex were measured. The obtained results showed that 1-BP led to cognitive dysfunction of rats, which was evidenced by delayed escape latency time and swimming distances in MWM performance. GSH and total-SH content, GSH/GSSG ratio, GR activity significantly decreased in cerebral cortex of rats, coupling with the increase of MDA level. 4-HNE and MDA modified protein levels obviously elevated after 1-BP exposure. GSH-Px activities in cerebral cortex of rats also increased. These data suggested that 1-BP resulted in enhanced lipid peroxidation of brain, which might play an important role in CNS damage induced by 1-BP.'

- Results: Did not affect memory function or motor coordination. Muscle strength decreased and increases in spontaneous locomotor activity. No data provided on lowest effect levels.
  Species: Rat.
  Exposure route: No information provided other than 'exposed' although inhalation likely, 8 hours/day, 7 days a week for 3 weeks.
  Method: Not stated.
  Reliability: Not stated.

'*Male F344 rats were exposed 8 hours/day, 7 days/week for 3 weeks at 10, 50, 200, or 1000 ppm 1-BP and evaluated for changes in behavior. Exposure to 1-BP did not affect memory function or motor coordination but muscle strength decreased dose-dependently. Dose-dependent increases in spontaneous locomotor activity and open-field behavior indicated that 1-BP has excitatory effects on the CNS of male F344 rats.*'

- Results: Decrease in limb strength and changes to motor nerve conduction and other CNS functions. Effects identified at 800 ppm (4.02 mg/L). No additional data provided on other lowest effect levels.
  Species: Rat.
  Exposure route: No information provided other than 'exposed' although inhalation likely, 8 hours/day for 12 weeks.
  Method: Not stated.
  Reliability: Not stated.

'*Wistar rats exposed 8 hours/day, 7 days/week for 12 weeks at 200, 400, or 800 ppm 1-BP exhibited dose-dependent decreases in fore limb and hind limb strength, motor nerve conduction velocities, plasma creatine phosphokinase, morphological changes in peripheral nerves and preterminal axons in the gracile nucleus, and increased distal latency of peripheral nerves. Ovoid or bubble-like debris of myelin sheaths was prominent in the unraveled muscular branch of the posterior tibial nerve observed in the 800-ppm group but not in the 200- or 400-ppm groups. Dose-dependent decreases in neuron-specific gamma-enolase and creatine kinase activities in the cerebrum and brain glutathione and nonprotein sulfhydryl levels were also observed.*'

- Results: Decreases in motor nerve conduction velocities, increased latency of peripheral nerves and neuronal dysfunction of the brain. No data provided on lowest effect levels.

Species: Rat.
Exposure route: No information provided other than 'exposed' although inhalation likely, 4 to 7 weeks.
Method: Not stated.
Reliability: Not stated.

'*Wistar rats exposed at 1,000 and 1,500 ppm 1-BP for 4 to 7 weeks exhibited decreases in body weight and motor nerve conduction velocities, increased distal latency of peripheral nerves, and neuronal dysfunction in the dentate gyrus of the brain.*'

- Results: Reduction in weights of cerebrum and gastrocnemius muscle for 800 ppm group. Reduced plasma creatine phosphokinase activities for 400 and 800 ppm groups. Other CNS changes. NOAEC = 200 ppm (1.0 mg/L).
  Species: Rat.
  Exposure route: Inhalation, 8 hours/day, 7 days a week for 12 weeks.
  Method: Not stated.
  Reliability: Not stated.

'*...A study to examine the dose- and duration- neurotoxicity response to 1-BP exposure /was conducted/. Eleven 10-week-old male Wistar rats/group ...were exposed to air or 200, 400, or 800 ppm [1,006, 2,012, or 4,025 mg/cu m] 1-BP vapors 8 hr/day for 12 weeks. Exposures were conducted 7 days per week under dynamic conditions. The highest nominal concentration was based on preliminary studies that noted debilitation of rats exposed to 1,000 ppm. ...Neurological function was tested in 9 rats/group at weeks 0, 4, 8, and 12. ...Mean bodyweights for the 400 and 800 ppm groups were significantly lower than controls after 8 weeks of exposure. Significant decreases in hindlimb grip strength were observed for all groups at 4 weeks, and for the 800 ppm group at 8 and 12 weeks. Hindlimb grip strength was also decreased for the 400 ppm group at 12 weeks. Significant decreases in forelimb grip strength were seen for the 400 and 800 ppm groups at 8 weeks, and for the 800 ppm group at 12 weeks. (The Expert Panel only considered reductions in grip strength to be treatment-related if they were statistically significant and consistently related to duration of treatment. Therefore, reductions in hindlimb grip strength and forelimb grip strength were considered treatment related at > or =400 ppm and 800 ppm, respectively.) MCV was reduced for the 800 ppm group at weeks 8 and 12, and distal latency (DL) was increased for this group at weeks 4, 8, and 12. The rats in the 800 ppm group also displayed weak kicking and an inability to stand on a slope. At sacrifice, brain weight and blood chemistry were analyzed from 9 animals per group. At necropsy, two animals from each group were perfused for neurohistopathology with either 10% formalin or Zamboni's solution (one for each fixative). Muscular nerves were dissected out and post-fixed in osmium tetroxide. The weights of the cerebrum and gastrocnemius muscle were significantly reduced for the 800 ppm group. No differences in weight were seen for other parts of the brain or soleus muscle. Plasma creatine phosphokinase activities for the 400 and 800 ppm groups were significantly reduced compared with controls. No changes were seen in the activities of lactate dehydrogenase, aspartate transaminase, alanine transferase, or alkaline phosphatase. Serum cholesterol was reduced in a dose-dependent manner, and plasma total protein and albumin were increased in a dose-related manner. Significant differences in cholesterol, aspartate*

transaminase, and alanine transaminase were seen for the 400 and 800 ppm groups. Plasma globulin levels were also significantly increased for the 800 ppm group. Morphological evidence of neurotoxicity was only noted in the high dose group (800 ppm) and included ovoid or bubble-like debris in myelin sheaths of peripheral nerves, swelling of preterminal axons of the gracile nucleus, and irregular banding of soleus muscle fibers. There was no degeneration or vacuolation of brain tissue. Authors noted that reductions in grip strength could not be explained by adverse changes in the nervous system alone, in that grip strength represents total vital factors in limb function. In comparing the result of this study to those obtained in a preliminary study with 2-BP, the authors concluded that 1-BP is a more potent neurotoxicant than 2-BP and is potentially neurotoxic to humans. (The Expert Panel determined a subchronic inhalation neurotoxicity NOAEC of 200 ppm.)'

Data Summary:

The European Commission assigned nPB a hazard phrase of H373 which equates to a moderate level of concern in the GreenScreen criteria. The affected organs identified in the European Chemicals Agency (ECHA) harmonised GHS classification included the Central Nervous System (CNS). In the GreenScreen criteria, H373 is used to identify repeat dose systemic toxicity concerns. However, impacts to the CNS indicate it also is appropriate for the repeat dose neurotoxicity evaluation.

The NIH's Hazardous Substances Databank (HSDB) listed eleven repeated dose studies, all of which identified some level of impacts to the central nervous system. Impacts ranged from impacts on nerves, negative impacts to the brain and decreased motor and cognitive function. Most effects were seen in the 200 to 800 ppm (1 to 3 mg/L) range. The only study that specifically calculated a NOAEC reported a value of 200 ppm (1.0 mg/L). Several additional studies reported impacts at slightly higher levels. These results are indicative of a Category 2 using GHS criteria which equates to a moderate level of concern in the GHS criteria and supports the hazard phrase determination by the European Commission.

Based upon these results, nPB was assigned a score of moderate for repeated dose neurotoxicity.

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

nPB was assigned a score of LOW for skin sensitization based on a single, valid study reported by the European Chemicals Agency. As there is limited data, the level of concern is italicized in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:* None
  - *Screening:* None

- ECHA, 2015.
  - Results: Non-sensitizing. No cutaneous reactions possibly attributable to the test substance were observed.
    Species: Guinea pig.

Exposure route: Dermal.
Method: OECD 406 and to GLP standard.
Reliability: Reliable without restriction - Study conducted in compliance with agreed protocols, with no or minor deviations from standard test guidelines and/or minor methodological deficiencies, which do not affect the quality of the relevant results.

'*A skin sensitization study according to the maximisation method of Magnusson and Kligman was performed on female Dunkin-Hartley guinea-pigs weighing 343 ± 22 g. The study was performed using the test substance 1-bromopropane and in accordance with OECD 406 and to GLP standard. No cutaneous reactions possibly attributable to the sensitization potential of the test substance were observed and the material is therefore not classed as a sensitizer, 1995.*'

nPB was assigned a score of low for skin sensitization based on limited data, specifically one study reported by the European Chemicals Agency (ECHA) identifying nPB as non-sensitizing. This study, however, followed OECD guidelines and met all data requirements, i.e. reliable without restrictions.

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

nPB was assigned a score of **DATA GAP** for respiratory sensitization based on lack of data for both nPB and the identified analog.

- Authoritative and Screening Lists
  - *Authoritative:* None
  - *Screening:* None

Data Summary:

nPB was assigned a score of data gap for respiratory sensitization based on lack of data.

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

nPB was assigned a score of **HIGH** for skin irritation/corrosivity based on two authoritative sources, the European Commission and the European Chemicals Agency assigning the risk and hazard phrases of R38, irritating to skin, and H315, causes skin irritation, respectively. As these determinations were made by authoritative sources, the high level of concern is bolded in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:*
    - EC - Risk Phrases - R38: Irritating to skin (Pharos)
  - *Screening:* None
- NIH National Library of Medicine Hazardous Substances Databank

- Result: '*... It is reported to be irritating to skin and eyes of mice ...*'

- ECHA, 2015.
  - H315: Causes Skin Irritation
  - R36/37/38 – Irritating to eyes, respiratory system and skin
  - Results: Non-irritant.
    Species: Albino rabbits.
    Exposure route: Dermal.
    Method: Federal Hazardous Substances Act Regulations, Federal Register vol. 33, section 1500.41.
    Reliability: Reliable with restrictions – Study conducted in accordance with generally accepted scientific principles, possibly with incomplete reporting or methodological deficiencies, which do not affect the quality of the relevant results.

  '*An acute dermal irritation study was performed on 1-bromopropane using 6 albino rabbits with weights from 2 - 3 kg (24 hour exposure, tests sites both intact and abraded) representing a worst case scenario for assessing irritation. Edema was observed in one out of the six animals tested. No eschar formation was observed. Propylbromide is considered as a nonirritant, 1978.*'

Data Summary:

The European Commission (EC) assigned nPB a Risk Phrase of R38, irritating to the skin. This equates to a high level of concern using the GreenScreen criteria. This determination is supported by a similar Risk Phrase assigned by the European Chemicals Agency (ECHA) which assigned nPB a Health Hazard Phrase of H315, causes skin irritation. H315 also equates to a high level of concern in the GreenScreen criteria. This determination is further supported by a scientific study in the NIH's Hazardous Substances Databank identifying nPB as irritating to the skin of mice.

One study reported by ECHA indicated that nPB is a non-irritant. This study, however, dates from 1978 and ECHA indicated that the study was reliable but with restrictions. The restrictions are not quantified but are likely due to the age of the study and potential deviations from current methodologies.

nPB was assigned a score of high for skin irritation/corrosivity based on identification of concerns both by EC and ECHA.

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

nPB was assigned a score of **HIGH** for eye irritation/corrosivity based on the European Commission and European Chemicals Agency assigning a hazard state of H319 (causes serious eye irritation) and R36 (irritating to the eyes), respectively. As these sources are authoritative, the high level of concern is bolded within the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists

- *Authoritative:*
  - EC - CLP/GHS Hazard Statements - H319 Causes serious eye irritation (Pharos)

- *Screening:* None

- NIH National Library of Medicine Hazardous Substances Databank
  - Result: '*The substance is irritating to the eyes and the respiratory tract.*'

  - Result: '*... It is reported to be irritating to skin and eyes of mice ...*'

- ECHA, 2015
  - R36/37/38 – Irritating to eyes, respiratory system and skin
  - Result: Irritant.
    Species: Rabbits.
    Exposure route: Application to the eye.
    Method: Consumer Product Safety Commission, Federal Register vol. 38, No. 187, 1500.42.
    Reliability: Reliable with restrictions – Study conducted in accordance with generally accepted scientific principles, possibly with incomplete reporting or methodological deficiencies, which do not affect the quality of the relevant results.

  '*An acute eye irritation study was performed on 6 male rabbits weighing at least 2 kg. Grading of eye irritation was according to the scale of Draize and the Illustrated Guide for Grading Eye Irritation published by the F.D.A. Scoring method was that of the Consumer Product Safety Commission, Federal Register vol. 38, No. 187, 1500.42. Since two out of the six animals tested exhibited a positive reaction, the test was repeated using a group of six different rabbits. The second test was considered positive since three animals out of six tested exhibited positive reactions. Propyl bromide is considered an eye irritant, 1978.*'

Data Summary:

The European Commission assigned nPB a Hazard Phrase of H319, causes serious eye irritation. This equates to a high level of concern using the GreenScreen criteria. The European Chemicals Agency (ECHA) supported this determination and assigned nPB a Risk Phrase of R36 which equates to either a high or moderate level of concern.

ECHA provides additional information by indicating nPB is an eye irritant which indicates a high level of concern. ECHA does include information from a 1978 study which indicated nPB is an eye irritant. This information is valid with restrictions, likely due to its age.

The NIH's Hazardous Substances Databank supports these determinations by identifying nPB as an eye irritant.

nPB was assigned a score of high for eye irritation/corrosivity based on determinations by the European Commission and the European Chemicals Agency as an eye irritant.

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M or L): **M**

nPB was assigned a score of **MODERATE** for acute aquatic toxicity based on identification by Japan METI/MOE, scientific studies and predicted results. As scientific studies were used for this determination, the moderate level of concern is bolded in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:* None
  - *Screening:*
    - Japan METI/MOE - GHS Classifications - Hazardous to the aquatic environment (acute) - Category 3 (Pharos)

- NIH National Library of Medicine Hazardous Substances Databank
  - Results: LC_{50} = 67.3 mg/L, 96 hour:
    Species: Pimephales promelas (Fathead minnow).
    Exposure route: Flow through.
    Method: Not stated.
    Reliability: Not stated.

- ECHA, 2015.
  - Results: LC_{50} > 67.3 mg/L; 96 hour:
    Species: Pimephales promelas (Fathead minnow).
    Exposure route: Not stated.
    Method: OECD Guideline 203 (Acute Toxicity Test).
    Reliability: Reliable with restrictions.

  - Results: LC_{50} = 18 mg/L; 96 hour:
    Species: Cyprinodon variegates.
    Exposure route: Not stated.
    Method: (Q)SAR results.
    Reliability: Reliable without restriction, data from US EPA generated by scientifically validated software, fully adequate for assessment.

  - Results: LC_{50} > 67 mg/L; 96 hour:
    Species: Oryzias latipes.
    Exposure route: Not stated.
    Method: OECD Guideline 203 (Fish, Acute Toxicity Test), read-across from supporting substance (structural analogue or surrogate).
    Reliability: Value generated by reading across experimental data, generated by a GLP compliant study, on the isomer 2-Bromopropane (CAS Nr. 75-26-3). Data adequate for assessment.

- Results: EC_{50} = 99.3 mg/L; 48 hour:
  Species: Daphnia magna under static conditions.
  Exposure route: Not stated.
  Method: OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test).
  Reliability: Study conducted in compliance with agreed protocols, with no or minor deviations from standard test guidelines and/or minor methodological deficiencies, which do not affect the quality of the relevant results**.**

Daphnids were exposed to 1-bromopropane dissolved in Elendt M4 medium at mean measured concentrations of 0, 5.22, 6.24, 13.2, 29.6 and 58.8 mg/L for 48 hours.

- Results: LC_{50} = 24.3 mg/L; 96 hour:
  Species: *Oncorhynchus mykiss*.
  Exposure route: Not stated.
  Method: Not stated.
  Reliability: Not stated.

In an acute toxicity to fish study (TSH0095), Oncorhynchus mykiss were exposed to 1-bromopropane for 96 hours under semi-static conditions in a sealed environment to prevent the volatile test substance from escaping. The 96-hour LC_{50} value for n-BP with rainbow trout was 24.3 mg/L, with 95% confidence limits of 17.7 and 33.3 mg/L.

- Results: LC_{50} = 24.3 mg/L; 48 hour:
  Species: Daphnia magna.
  Exposure route: Aqueous.
  Method: Not stated.
  Reliability: Not stated.

The 48 hr-acute toxicity of 1-bromopropane to Daphnia magna was studied under static conditions. Daphnids were exposed to 1-bromopropane dissolved in Elendt M4 medium at mean measured concentrations of 0, 5.22, 6.24, 13.2, 29.6 and 58.8 mg/L for 48 hours. The 48 hour EC_{50} based on immobility was 99.3 mg/L. No 95% confidence intervals could be determined.

- Results: EC_{50} > 54.98 mg/L; 72 hour:
  Species: Freshwater algae *(Selenastrum capricornutum).*
  Exposure route: Aqueous.
  Method: Not stated.
  Reliability: Study conducted in accordance with generally accepted scientific principles, possibly with incomplete reporting or methodological deficiencies, which do not affect the quality of the relevant results.

In an acute toxicity to algae study, Freshwater algae (Selenastrum capricornutum) was exposed to 1-bromopropane for 72 hours at measured initial concentrations of 54.98, 20.97, 8.53, 4.82, 1.65 and 0.93 mg/L. The 72 hour growth rate EC_{50} value for 1-bromopropane was determined to be > 54.98 mg/L.

- OECD, 2015.
  - Reporting LC_{50} modeling results, 96 hour unless otherwise noted:
    - LC_{50} = 83.5 mg/L; predicted for fathead minnow by Topkat v 6.1
    - LC_{50} = 64.5 mg/L; predicted for fish by Ecosar v0.99g
    - LC_{50} = 159.4 mg/L; predicted for fish by Oasis Forecast M v1.10
    - LC_{50} = 19.9 mg/L; predicted for fish by PN
    - EC_{50} = 333.9 mg/L; predicted for daphnia by Topkat v 6.1
    - LC_{50} = 16.6 mg/L (in LC_{50} or EC_{50}); predicted for fish, daphnia, algae or mysid shrimp by Ecosar v0.99g
    - LC_{50} = 64.5 mg/L; predicted for fish by Neutral Organics QSAR in Ecosar v0.99g

Data Summary:

The Japanese METI/MOE assigned nPB a Category 3 GHS classification which equates to a moderate level of concern using the GreenScreen criteria. This list, however, is used as a screening evaluation and needs to be supported with other data. The NIH's Hazardous Substances Databank (HSDB) reported a study with an LC_{50} = 67.3 which equates to a moderate level of concern.

The European Chemicals Agency (ECHA) reported several studies and modeling results, all of which reported LC_{50} (ranging from 18 to 24.3 mg/L) and EC_{50} (99.3 mg/L) values within the moderate level of concern using GreenScreen criteria. Two studies reported values in the same range but were limited to 'greater than' and could not be used to identify a level of concern.

Similar predictive results were reported by the Organisation for Economic Cooperation and Development (OECD). Four of the predicted values ranged from 16.6 to 83.5 mg/L (moderate level of concern) while two, LC_{50} = 159.4 and EC_{50} = 333.9 mg/L, identified a low level of concern using the GreenScreen criteria.

nPB was assigned a score of moderate for acute aquatic toxicity based on identification by the Japan METI/MOE, studies reported by ECHA and predictive results reported by the OECD.

.

Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): *M*

nPB was assigned a score of **MODERATE** for chronic aquatic toxicity based on screening results from the Japan METI/MOE, EPA and ECHA. As the level of concern is based upon an screening results, it is italicized in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:* None

  - *Screening:*
    - Japan METI/MOE - GHS Classifications - Hazardous to the aquatic environment (chronic) - Category 3 (Pharos)

- EPA, 2012.
  - PBT Profiler: Fish ChV = 7.2 mg/L.

- ECHA CLP, 2015.
  - Result: H412, Aquatic Chronic 3.
  - Result: H412, Aquatic Chronic 4.
  - Result: H412, Aquatic Chronic 3.

Data Summary:

Japan METI/MOE identified nPB as a Category 3 toxicant, chronic hazard to the aquatic environment. This identification, however, is not used by the GreenScreen criteria to identify a level of concern. EPA in its PBT Profiler predicted a chronic toxicity for nPB (Fish ChV = 7.2 mg/L) which equates to a moderate level of concern.

Three companies reported to the European Chemicals Agency (ECHA) as part of the REACH Classification and Labelling requirements that nPB should be assigned a Hazard Statement of H412, Aquatic Chronic 3. This data has not been validated by ECHA and therefore is taken as a screening result until validation occurs. The H412 Hazard Statement, however, translates into a moderate level of concern which supports other screening and modeling results.

nPB was assigned a score of moderate for chronic aquatic toxicity based screening results from several sources including the Japan METI/MOE, EPA's PBT Profiler and the ECHA CLP database.

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): *H*

nPB was assigned a score of **HIGH** for persistence based on identification by Environment Canada as a persistent chemical and prediction by EPA as persistent in air. As the level of concern is based primarily upon predictions, it is italicized in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:* None

  - *Screening:*
    - Environment Canada - Domestic Substances List - DSL substances that are Persistent (Pharos)

- HSDB, 2015.
  - Water, $t_{1/2}$ (half life) = 3. hours or 4.4 days (modeled)
  - Water, $t_{1/2}$ (half life) = 26 days (predicted)

- Air, $t_{1/2}$ (half life) = 15 days (predicted)

'*Based on a classification scheme, an estimated K_{oc} value of 40, determined from a structure estimation method, indicates that 1-bromopropane is not expected to adsorb to suspended solids and sediment. Volatilization from water surfaces is expected based upon an estimated Henry's Law constant of 7.3X10-3 atm-cu m/mole, derived from a vapor pressure of 111 mm Hg and water solubility of 2450 mg/L. Using this Henry's Law constant and an estimation method, volatilization half-lives for a model river and model lake are 3.4 hours and 4.4 days, respectively. The hydrolysis half-life of 1-bromopropane is approximately 26 days at pH 7 and 25 deg C. A 70% of theoretical BOD using activated sludge in the Japanese MITI test suggests that biodegradation may an important environmental fate process in water. A number of pure culture studies have shown that microorganisms are capable of degrading 1-bromopropane.*'

The rate constant for the vapor-phase reaction of 1-bromopropane with photochemically produced hydroxyl radicals has been measured as 1.06X10-12 cu cm/molecule-sec at 25 deg C(1). This corresponds to an atmospheric half-life of about 15 days at an atmospheric concentration of 5X10+5 hydroxyl radicals per cu cm. An aqueous hydrolysis half-life of about 26 days was calculated based upon a neutral hydrolysis rate measured at 55 deg C for 1-bromopropane at pH 7 and 25 deg C from its first-order rate constant of 3.01X10-7 sec-1(2).

- EPA, 2012.
  - PBT Profiler
    - Water, $t_{1/2}$ (half life) = 15 days, 44% of media
    - Soil, $t_{1/2}$ = 30 days, 10% of media
    - Sediment, $t_{1/2}$ = 140 days, 0% of media
    - Air, $t_{1/2}$ = 14 days, 46% of media

- CERHR, 2003.

There is very little information documenting the presence of n-PB in ambient air, drinking or surface waters, food, or consumer products. An unspecified level of n-PB was detected in the drinking water from an unreported location. Schwarzenbach et al. reported on an investigation of leaks from a wastewater tank at a Swiss alkyl halide factory at which n-PB was manufactured (>5 tons/year). After the plant ceased operation, the underlying aquifer was found to be heavily polluted. Following soil excavation and continuous groundwater pumping for 7 years, substantial concentrations of bromobenzene and chlorobenzene were found, but neither n-PB, nor 2-BP, nor its corresponding alcohol metabolites could be detected in groundwater. In vitro studies by Schwarzenbach et al. confirmed the rapid hydrolysis of n-PB (half life of 26 days) under anaerobic conditions.

The atmospheric lifetime of n-PB is reported to be less than 20 days due to reactions with hydroxyl that result in the release of bromine atoms and formation of brominated acetone. Unreported levels of n-PB were detected in the volatile emissions from household waxes, liquid pastes, and detergents. n-PB was also detected in six species of marine microalgae at

unreported levels; it was postulated that the n-PB was a product of monohalo and dihalo-oxo-fatty acid hydrolysis and that it could be transported from the algae to the marine environment.

Data Summary:

Environment Canada identified nPB as a persistent substance. This equates into either a very high or high level of concern using the GreenScreen criteria. Using the PBT Profiler, EPA predicted that nPB would persist in air (half-life = 14 days, high level of concern) and soil (half-life = 30 days, moderate level of concern) and would not persist in soil (half-life = 15 days, low level of concern). These results were supported by a report from CERHR that identified an atmospheric half-life of 15 days.

nPB was assigned a score of high for persistence based on identification by Environment Canada as a persistent chemical and predictions by EPA and CERHR that nPB would persist in air. EPA also predicted that nPB would partition equally into air and water which account for 90% of the chemical released into the environment. As nPB is expected to persist air, high was selected as the level of concern.

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Bioaccumulation (B) Score (vH, H, M, L, or vL): *vL*

nPB was assigned a score of **VERY LOW** for bioaccumulation based on predicted values reported in a number of sources including the NIH's Hazardous Substances Databank, EPA's PBT Profiler and the Organisation for Economic Cooperation and Development. As the very low level of concern is based upon predicted results, it is italicized in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:* None
  - *Screening:* None

- NIH National Library of Medicine Hazardous Substances Databank
  - Result: BCF = 11.
    '*An estimated BCF of 11 was calculated in fish for 1-bromopropane (SRC), using a measured log K_{ow} of 2.1 and a regression-derived equation. According to a classification scheme, this BCF suggests the potential for bioconcentration in aquatic organisms is low(SRC). 1-Bromopropane was classified as having low bioconcentration based on fish accumulation studies (specific data not reported).*'

- EPA, 2012.
  - PBT Profiler: BCF = 11.

- OECD, 2015.
  - Log K_{ow} = 2.1 (Empirical).
  - Log K_{ow} = 2.16, predicted by K_{ow}Win.
  - Log BCF= 0.917, predicted by BCFWIN.

- Log BCF = 1.785, Max predicted by OASIS).
- Log BAF = 0.95, T@MTL predicted by Gobas.

- INCHEM, 2015:
  - Log K_{ow} = 2.1 (Empirical).

Data Summary:

nPB was assigned a score of very low for bioaccumulation based on predicted results reported in a number of sources. The NIH's Hazardous Substances Databank reported a BCF = 11 (very low level of concern) equivalent to the value reported by EPA's PBT Profiler. The Organisation for Economic Cooperation and Development (OECD) reported BCF and BAF values ranging from 0.917 to 1.785 which equate to a very low level of concern. The OECD also reports predicted log K_{ow} values of 2.1 and 2.16. Another source, INCHEM, reported the same log K_{ow} value of 2.1. All of these log K_{ow} values equate to a very low level of concern in the GreenScreen criteria.

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Physical Hazards

Reactivity (Rx) Score (vH, H, M or L): **M**

nPB was assigned a score of **MODERATE** for reactivity based on the New Jersey Department of Health's identification of Reactivity Rating equal to 1(*slight reactivity*) and the National Oceanographic and Atmospheric Administration Cameo Chemical's reactivity profile which indicated compounds such as nPB are '*moderately or very reactive*'. As the NJDOH and NOAA are authoritative sources, it is bolded in the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:* None
  - *Screening:* None

- New Jersey Department of Health (NJDOH), 2009
  - Reactivity Rating = 1 '*slight reactivity*'.

- PubChem, 2015.
  - Section 9.2.3 NFPA Hazard Classification
    Instability: 0. '… *normally stable, even under fire exposure conditions, and that do not react with water. Normal fire fighting procedures may be used.*'

- Fluorochem, 2011.
  - Section 10: Stability and Reactivity, 1. Reactivity: '*This material is stable if stored under proper conditions,*'

- TCI America, 2005.

- Section X: Stability and Reactivity, Stability: '*no unusual reactivity*'.

- Georgia Regents University (GRU), 2012.
  - NPFA Rating for Reactivity = 0, non-reactive.

- NOAA Cameo Chemicals, 2015
  - Instability = 0 '*Normally stable, even under fire conditions.*'
  - Reactivity Profile: '*Halogenated aliphatic compounds, such as 2-BROMOPROPANE, are moderately or very reactive. Halogenated organics generally become less reactive as more of their hydrogen atoms are replaced with halogen atoms. Low molecular weight haloalkanes are highly flammable and can react with some metals to form dangerous products. Materials in this group are incompatible with strong oxidizing and reducing agents. Also, they are incompatible with many amines, nitrides, azo/diazo compounds, alkali metals, and epoxides. Emits toxic fumes of bromine when burned.*'

Data Summary:

The New Jersey Department of Health identified nPB as 'slightly reactive' which was supported by the Safety Data Sheet (SDS) from a manufacturer, Fluorchem. PubChem, a publication of the US National Institute of Health, identified that nPB is normally stable and assigned a low level of instability concern. This conclusion was supported by a Material Safety Data Sheet (MSDS) from another manufacturer, TCI America, and a listing of toxic chemicals by Georgia Regents University which both indicated no reactivity.

Lastly, the National Oceanographic and Atmospheric Administration's (NOAA) Cameo Chemicals summary for nPB indicated that halogenated aliphatic compounds are moderately or very reactive while also indicating that nPB is '*normally stable, even under fire conditions.*'

Based upon the information above, either a low or moderate level of concern is appropriate for nPB; however, based upon the determinations by the New Jersey Department of Health and the NOAA's reactivity profile, it was assigned a score of moderate for reactivity.

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Flammability (F) Score (vH, H, M or L): **H**

nPB was assigned a score of **HIGH** for flammability based on the European Commission's assignment of the Hazard Statement of H225 as a highly flammable liquid. This determination was supported by data from other sources. As the high level of concern is based upon an authoritative source, it is bolded within the GreenScreen Hazard Summary Table.

- Authoritative and Screening Lists
  - *Authoritative:*
    - EC - CLP/GHS Hazard Statements - H225 Highly flammable liquid and vapour. (Pharos)

  - *Screening:*

- NJDOH (2009):
  - Flammability Hazard Summary, Rating = 3 '*serious flammability, 1-Bromopropane is a flammable liquid and a dangerous fire hazard.*'
    - Vapors may travel to a source of ignition and flash back.
    - Vapor is heavier than air and may travel a distance to cause a fire or explosion far from the source.
    - Flow or agitation may generate electrostatic charges.

- ECHA, 2015:
  - R11 – Highly flammable

- INCHEM, 2015:
  - Highly flammable. Gives off irritating or toxic fumes (or gases) in a fire.

Data Summary:

The European Commission assigned nPB a Hazard Statement of H225, highly flammable liquid and vapour. This equates to a high level of concern using the GreenScreen criteria. This determination is supported by the determination by the New Jersey Department of Health as a flammable liquid and a dangerous fire hazard with a rating of '3'.

The European Chemicals Agency (ECHA) assigned nPB the risk phrase, R11 and highly flammable. This equates to either a very high or high level of concern. Finally, INCHEM also identifies nPB as highly flammable.

nPB was assigned a score of high for flammability based on determination by the European Commission as highly flammable which is supported by three other sources.

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APPENDIX A: Hazard Benchmark Acronyms (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

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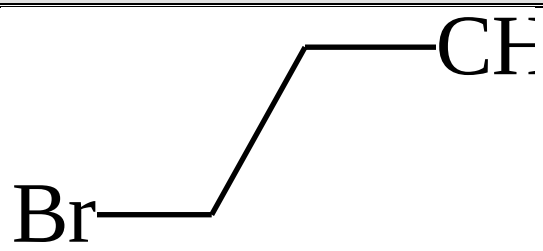
Appendix B
Modeling Results

EPI Suite Results For CAS 106-94-5



```
SMILES : BrCCC
CHEM   : 1-bromopropane
MOL FOR: C3 H7 Br1
MOL WT : 122.99
------------------------------ EPI SUMMARY (v4.11) -------------------------
Physical Property Inputs:
Log Kow (octanol-water):   ------
Boiling Point (deg C)  :   ------
Melting Point (deg C)  :   ------
Vapor Pressure (mm Hg) :   ------
Water Solubility (mg/L):   ------
Henry LC (atm-m3/mole) :   ------

Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.68 estimate) =  2.16
Log Kow (Exper. database match) =  2.10
Exper. Ref:  HANSCH,C ET AL. (1995)

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C):  77.57  (Adapted Stein & Brown method)
Melting Pt (deg C):  -79.08  (Mean or Weighted MP)
VP(mm Hg,25 deg C):  137  (Mean VP of Antoine & Grain methods)
VP (Pa, 25 deg C) :  1.83E+004  (Mean VP of Antoine & Grain methods)
MP  (exp database):  -110 deg C
BP  (exp database):  71.1 deg C
VP  (exp database):  1.11E+02 mm Hg (1.48E+004 Pa) at 20 deg C
```

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Water Solubility Estimate from Log Kow (WSKOW v1.42):
Water Solubility at 25 deg C (mg/L):  1574
log Kow used: 2.10 (expkow database)
no-melting pt equation used
Water Sol (Exper. database match) =  2450 mg/L (20 deg C)
Exper. Ref:  YALKOWSKY,SH & HE,Y (2003)

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) =  2371.2 mg/L

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

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method :   1.50E-002  atm-m3/mole  (1.52E+003 Pa-m3/mole)
Group Method:   1.14E-002  atm-m3/mole  (1.16E+003 Pa-m3/mole)
Exper Database: 7.32E-03  atm-m3/mole  (7.42E+002 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:  1.409E-002 atm-m3/mole  (1.427E+003 Pa-m3/mole)
VP:   137 mm Hg (source: MPBPVP)
WS:   1.57E+003 mg/L (source: WSKOWWIN)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
Log Kow used:  2.10  (exp database)
Log Kaw used:  -0.524  (exp database)
Log Koa (KOAWIN v1.10 estimate):  2.624
Log Koa (experimental database):  None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model)         :   0.6428
Biowin2 (Non-Linear Model)     :   0.0399
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model):   2.9563  (weeks       )
Biowin4 (Primary Survey Model) :   3.7057  (days-weeks  )
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model)    :   0.5422
Biowin6 (MITI Non-Linear Model):   0.3312
Anaerobic Biodegradation Probability:
```

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```
Biowin7 (Anaerobic Linear Model):  1.1676
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):  1.48E+004 Pa (111 mm Hg)
Log Koa (Koawin est  ): 2.624
Kp (particle/gas partition coef. (m3/ug)):
Mackay model           :  2.03E-010
Octanol/air (Koa) model:  1.03E-010
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model     :  7.32E-009
Mackay model           :  1.62E-008
Octanol/air (Koa) model:  8.26E-009

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant =   0.9186 E-12 cm3/molecule-sec
Half-Life =    11.644 Days (12-hr day; 1.5E6 OH/cm3)
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
1.18E-008 (Junge-Pankow, Mackay avg)
8.26E-009 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):
Koc    :  39.6  L/kg (MCI method)
Log Koc:  1.598       (MCI method)
Koc    :  66.4  L/kg (Kow method)
Log Koc:  1.822       (Kow method)

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
Total Kb for pH > 8 at 25 deg C :  4.509E-009  L/mol-sec
Kb Half-Life at pH 8: 4.870E+006  years
Kb Half-Life at pH 7: 4.870E+007  years
(Total Kb applies only to esters, carbmates, alkyl halides)

Bioaccumulation Estimates (BCFBAF v3.01):
```

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Log BCF from regression-based method = 1.053 (BCF = 11.29 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -0.6402 days (HL = 0.229 days)
Log BCF Arnot-Gobas method (upper trophic) = 1.068 (BCF = 11.69)
Log BAF Arnot-Gobas method (upper trophic) = 1.068 (BAF = 11.69)
log Kow used: 2.10 (expkow database)

Volatilization from Water:
Henry LC:  0.00732 atm-m3/mole  (Henry experimental database)
Half-Life from Model River:       1.22  hours
Half-Life from Model Lake :      106.3  hours   (4.429 days)

Removal In Wastewater Treatment:
Total removal:              74.39  percent
Total biodegradation:        0.04  percent
Total sludge adsorption:     0.99  percent
Total to Air:               73.36  percent
(using 10000 hr Bio P,A,S)

Level III Fugacity Model:
      Mass Amount    Half-Life    Emissions
      (percent)        (hr)       (kg/hr)
Air       44.1           218          1000
Water     45.7           360          1000
Soil      10.1           720          1000
Sediment  0.159          3.24e+003    0
Persistence Time: 138 hr
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Summary of prediction for models:
Mutagenicity model (CAESAR) (version 2.1.12)
Carcinogenicity model (CAESAR) (version 2.1.8)
Developmental Toxicity model (CAESAR) (version 2.1.6)
Skin Sensitisation model (CAESAR) (version 2.1.5)
Fathead Minnow LC_{50} 96h (EPA) (version 1.0.6)
Daphnia Magna LC_{50} 48h (EPA) (version 1.0.6)
BCF model (CAESAR) (version 2.1.13)
BCF model (Meylan) (version 1.0.2)
BCF Read-Across (version 1.0.2)
Ready Biodegradability model (version 1.0.8)
Log P prediction (version 1.1.2)
(calculation core version: 1.1.1)

Mol	Id	SMILES
1	Molecule 1	CCCBr

Mutagenicity model (CAESAR) - prediction	Suspect Mutagen
Mutagenicity model (CAESAR) - assessment	Suspect Mutagen (moderate reliability)
Carcinogenicity model (CAESAR) - prediction	NON-Carcinogen
Carcinogenicity model (CAESAR) - assessment	NON-Carcinogen (low reliability)
Developmental Toxicity model (CAESAR) - prediction	Toxicant
Developmental Toxicity model (CAESAR) - assessment	Toxicant (low reliability)
Skin Sensitisation model (CAESAR) - prediction	NON-Sensitizer
Skin Sensitisation model (CAESAR) - assessment	NON-Sensitizer (moderate reliability)
Fathead Minnow LC50 96h (EPA) - prediction	3.23 experimental
Fathead Minnow LC50 96h (EPA) - assessment	LC_{50} (96h) = 3.26 [-log(mol/l)]
Daphnia Magna LC50 48h (EPA) - prediction	2.83
Daphnia Magna LC50 48h (EPA) - assessment	LC_{50} (48h) = 2.83 [-log(mol/l)] (low reliability)
BCF model (CAESAR) – prediction	0.81
BCF model (CAESAR) - assessment	log BCF = 0.81 (good reliability)
BCF model (Meylan) - prediction	1.05
BCF model (Meylan) - assessment	log BCF = 1.05 (good reliability)
BCF Read-Across - prediction	1.01

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BCF Read-Across - assessment	log BCF = 1.01 (low reliability)
Ready Biodegradability model - prediction	NON Ready Biodegradable
Ready Biodegradability model - assessment	NON Ready Biodegradable (low reliability)
LogP prediction - prediction	2.16 experimental
LogP prediction – assessment	log P = 2.1