Isopropanol (CAS# 67-63-0) GreenScreen® for Safer Chemicals (GreenScreen®) Assessment

Prepared by:

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GreenScreen® Executive Summary for Isopropanol (CAS #67-63-0)

Isopropanol is a chemical that functions as a stabilizer and winterizing agent in hydraulic fracturing fluids, as a solvent, a denaturing agent, a chemical intermediate for organic synthesis, and a disinfectant.

Isopropanol was assigned a GreenScreen® Benchmark Score of 2 ("Use but Search for Safer Substitutes") as it has Moderate Group I Human Toxicity (reproductive toxicity (R) and developmental toxicity (D)), Very High Group II Human Toxicity (systemic toxicity single exposure (STs)), High reactivity (Rx) and High flammability (F). This corresponds to GreenScreen® benchmark classification 2e, f and g in CPA 2011. Data gaps (DG) exist for endocrine activity (E) and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), isopropanol meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if isopropanol were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical. If it were assigned a High score for SnR*, isopropanol would still be categorized as a Benchmark 2 Chemical.

GreenScreen® Benchmark Score for Relevant Route of Exposure:

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

GreenScreen® Hazard Ratings for Isopropanol

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

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

GreenScreen® Assessment for Isopropanol (CAS #67-63-0)

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

Chemical Name: Isopropanol

CAS Number: 67-63-0

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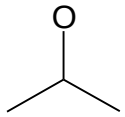
Organization: ToxServices LLC
Date: June 25, 2014

Confirm application of the *de minimus* rule[1]: N/A

Chemical Structure(s):



Isopropanol (CAS#67-63-0)

Also called: 2-Propanol; Isopropyl alcohol, 1-Methylethanol; 1-Methyl alcohol; 2-Hydroxypropane; n-Propan-2-ol; 2-Propyl alcohol (ChemIDplus 2014)

Chemical Structure(s) of Chemical Surrogates Used in the GreenScreen®:
Isopropanol has a relatively complete dataset that satisfied the minimum requirements for its benchmark level. Therefore, no surrogates were sought.

Identify Applications/Functional Uses:
1. Routinely used in hydraulic fracturing as a stabilizer and/or winterizing agent in corrosion inhibitors, non-emulsifiers and surfactants. A typical water-based hydraulic fracturing fluid contains isopropanol at 0.085%.
2. Solvent in food, pharmaceuticals and personal care products
3. Denaturing agent in specimen preparation
4. Chemical intermediate for organic synthesis
5. Disinfectant for home, hospital and industry (HSDB 2012)

GreenScreen® Summary Rating for Isopropanol[2]: Isopropanol was assigned a GreenScreen® Benchmark Score of 2 ("Use but search for safer substitutes") as it has Moderate Group I Human

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

Toxicity (reproductive toxicity (R) and developmental toxicity (D)), Very High Group II Human Toxicity (systemic toxicity single exposure (STs)), High reactivity (Rx) and High flammability (F). This corresponds to GreenScreen® benchmark classification 2e, f and g in CPA 2011. Data gaps (DG) exist for endocrine activity (E) and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), isopropanol meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if isopropanol were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical. If it were assigned a High score for SnR*, isopropanol would still be categorized as a Benchmark 2 Chemical.

Figure 1: GreenScreen® Hazard Ratings for Isopropanol

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

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

Transformation Products and Ratings:

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

No feasible and relevant environmental transformation products were identified for isopropanol.

Introduction

Isopropanol is an aliphatic alcohol hydrocarbon. It is prepared from propylene, which comes from the cracking of petroleum or from reduction of acetone. It has a slight odor resembling ethanol and acetone, and has a slight bitter taste. Isopropanol has little absorption through intact skin, but prolonged exposure can lead to some absorption. Oral absorption is complete within 2 hours. The majority of absorbed isopropanol is oxidized by liver alcohol dehydrogenase to acetone, formate and ultimately carbon dioxide. Excretion of acetone mainly occurs through the lung and kidney (HSDB 2012).

ToxServices assessed isopropanol against GreenScreen® Version 1.2 (CPA 2013) following procedures outlined in ToxServices' SOP 1.37 (GreenScreen® Hazard Assessment) (ToxServices 2013).

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

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

GreenScreen® List Translator Screening Results

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

PhysicoChemical Properties of Isopropanol

Isopropanol is a highly volatile colorless liquid at room temperature. It is highly soluble in water and the partition coefficient of less than 1 indicates that it is hydrophilic.

Table 1: Physical and Chemical Properties of Isopropanol (CAS #67-63-0)

Property	Value	Reference
Molecular formula	C_3H_8O	ChemIDplus 2014
SMILES Notation	C(C)(C)O	ChemIDplus 2014
Molecular weight	60.0952	ChemIDplus 2014
Physical state	Liquid	HSDB 2012
Appearance	Colorless liquid	HSDB 2012
Melting point	-87.9ºC	HSDB 2012
Vapor pressure	45.4 mmHg at 25ºC	HSDB 2012
Water solubility	Infinitely soluble at 25ºC	HSDB 2012
Dissociation constant	pKa = 17.10	HSDB 2012
Density/specific gravity	0.78509 at 25ºC	HSDB 2012
Partition coefficient	0.05	HSDB 2012

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

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

Isopropanol was assigned a score of Low for carcinogenicity based on lack of evidence in animals and humans. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate data are available and negative, there are no structural alerts, and they are not classifiable under GHS (CPA 2012a).

- Authoritative and Screening Lists
  - Not present on any authoritative or screening lists.
- IARC 2012
  - Cancers in the nasal cavity were observed in workers during manufacture of isopropanol by the strong-acid processes. Isopropanol is manufactured by three methods: indirect hydration of propylene, direct hydration of propylene and catalytic hydrogenation of acetone. In the indirect-hydration method, there are two processes, the strong acid process which uses sulfuric acid at high concentrations (>80% wt) and low temperature

(20-30ºC), and the weak-acid process which uses a lower concentration of acid (60 – 80%) at higher temperatures (60 – 65ºC). A plausible mechanism of carcinogenesis of the strong-acid process to produce isopropanol involves the inhalation of inorganic acid mists that causes DNA damage. There are no data available to evaluate the carcinogenicity of strong acid mists in experimental animals. It was concluded that isopropanol manufacture by the strong-acid process is carcinogenic to humans (Group I).

- IARC 1999
  - Increased incidences of paranasal sinuses and laryngeal cancers were reported where isopropanol was manufactured by the strong-acid process. However, one case-control study did not find an association of occupational isopropanol exposure and increased cancer incidences.
  - One study with limitations in design and adequacy did not find increased tumor incidences in mice but found a slight increase in interstitial cell adenomas of the testis in male rats after chronic inhalation to isopropanol.
  - It was concluded that there is inadequate evidence for carcinogenicity of isopropanol in humans and in experimental animals.
- ECHA 2014
  - A GLP-compliant inhalation oncogenicity study was conducted according to OECD guideline 451 in F344 rats and CD-1 mice. Animals were exposed to isopropanol vapor via whole body inhalation at 0, 500, 2,500 or 5,000 ppm for 6 hours/day, 5 days/week for 104 weeks (rats) and 78 weeks (mice). In rats (65/sex/dose for the core group and 10/sex/dose for interim sacrifice), there was a dose-related increase in interstitial cell adenomas of the testis at interim and terminal sacrifices and in males that died during the study. The authors stated that testicular adenomas are common in aged male rats with a historical incidence rate of 88% in studies conducted by the National Toxicology Program (NTP), while the incidence in control rats in the current study was 64.9%. Therefore, this tumor was considered to be possibly spurious by the study authors. In mice (55/sex/dose for the core group, 10/sex/dose for the interim sacrifice group and 10/sex/dose for recovery group), no treatment-related neoplastic lesions were found (Burleigh-Flayer H et al. 1997 as cited in ECHA 2014).
- Based on the weight of evidence, isopropanol itself is not likely to be a carcinogen.

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

Isopropanol was assigned a score of Low for mutagenicity/genotoxicity based on negative data for mutagenicity and chromosome aberration *in vitro* and *in vivo*. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when adequate data are available and negative for both chromosomal aberration and gene mutation, there are no structural alerts, and they are not classifiable under GHS (CPA 2012a).

- Authoritative and Screening Lists
  - Not present on any authoritative or screening lists.
- ECHA 2014
  - A non-GLP bacterial reverse mutation assay was conducted using a protocol similar to OECD guideline 471. Isopropanol was not mutagenic in *S. typhimurium* tester strains TA97, TA98, TA100, TA1535 and TA1537 at concentrations of up to 10,000 µg/plate with and without metabolic activation (Zeiger et al. 1992 as cited in ECHA 2014).
  - A GLP-compliant mammalian cell gene mutation assay was conducted according to OECD guideline 476. Isopropanol was not mutagenic in Chinese hamster Ovary (CHO) cells at concentrations of up to 5.0 mg/mL in the presence and absence of metabolic

activation (Report date 1990).
    - A GLP-compliant *in vivo* micronucleus assay was conducted according to OECD guideline 474. ICR mice (15/sex/dose) received isopropanol via single intraperitoneal injection at 0, 350, 1,173, 2,500 or 3,500 mg/kg. There was no significant increase in micronucleated polychromatic erythrocytes in the bone marrow (Report date 1991).

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

Isopropanol was assigned a score of Moderate for reproductive toxicity based on classification to GHS category 2 with limited evidence in animals. GreenScreen® criteria classify chemicals as a Moderate hazard for reproductive toxicity when they are classified to GHS category 2 (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not on any authoritative lists
    - *Screening:* GHS-Japan: toxic to reproduction category 2
- ECHA 2014
    - A GLP-compliant 2-generation reproductive toxicity study was conducted according to OECD guideline 416. Isopropanol was administered to Sprague-Dawley rats via daily gavage at 0, 100, 500 or 1,000 mg/kg/day. There was no treatment related changes in body weight, food consumption, reproductive performance, gross pathology and histopathology in parental animals. Absolute and relative liver weights were statistically significantly increased in high does P1 males. Relative liver weight was increased in the mid and high dose females, and relative kidney weight was increased at the high dose only in females. The NOAEL for reproductive toxicity was established at 1,000 mg/kg/day by ECHA based on lack of reproductive effects (Report date 1992).
    - A GLP-compliant 1-generation reproductive toxicity study was conducted according to OECD guideline 415. Isopropanol was administered to Wistar rats in drinking water at 0, 0.5, 1.0 or 2.0%. There were no deaths, abortions, early deliveries or dams removed from the study. Reduced water intake was observed in males at all doses, but was transient only at the lowest dose. There was also a dose-related decrease in food consumption, but body weight gain was not significantly affected in males. In females, water and food consumption decreased at the mid and high doses prior to mating, and the reduction persisted to lactation period at the high dose. There was no treatment related effect on male and female fertility and the length of gestation in females. The number of pups/litter on gestation day 1 decreased at the high dose. Since this effect was not replicated in the embryotoxicity portion of the study, it was proposed that pup mortality was increased during parturition of gestation 0 followed by cannibalism of the dead pups by the dam. A slight dose-dependent reduction in red blood cells was found in males at the high dose and in females at the mid and high doses. The mean cell volume in the mid and high doses was also decreased in males. A statistically significant increase was found in absolute kidney weight and relative kidney, liver and spleen weights in F0 high dose males, and in absolute liver and kidney weights and relative liver weights in F0 females. Increased pre-implantation loss, decreased mean litter weight and mean fetal body weight were observed at the high dose. ECHA reported a NOAEL of 0.5% for parental systemic toxicity based on reduced food and water intake, reduced body weight, changes in red blood cells and cell volume and organ weight changes to liver, kidney and spleen. A NOAEL of 1% (853, 1,330 and 1,948 mg/kg/day for females during premating, gestation and postpartum phases, respectively) was reported for reproductive toxicity based on increased pre-implantation loss, decreased mean litter weight and mean fetal body weight (Report date: 2008).

  - A GLP-compliant 1-generation reproductive toxicity study was conducted according to OECD guideline 415. Wistar rats received isopropanol in drinking water at 0, 0.5, 1.25, 2 or 2.5%. Reduced water intake was found at concentrations of 1.25 and above. Body weight was reduced at 2.0 and 2.5% in both sexes. There was 100% fertility, but also evidence of embryotoxicity as demonstrated by less pups produced, increased pup mortality and reduced pup weight gain at 2.0 and 2.5%. There were signs of anemia in females and all rats had increased liver and kidney weights at doses of 1.25% and higher (Report date: 1986).
- Based on the weight of evidence, increased pre-implantation loss, reduced number of pups produced, increased pup mortality, and decreased mean litter weight and mean fetal body weight were observed in 1-generation drinking water studies, but not in the 2-generation gavage study. Limited evidence of effects in animals classifies isopropanol to GHS category 2.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): M
Isopropanol was assigned a score of Moderate for developmental toxicity based on classification to GHS category 2. GreenScreen® criteria classify chemicals as a Moderate hazard for developmental toxicity when they are classified to GHS category 2 (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* German MAK: Pregnancy Risk Group C
  - *Screening:* GHS-Japan: toxic to reproduction category 2 (includes effects on development)
- ECHA 2014
  - In the two-generation gavage toxicity study described above, increased mortality was observed with high dose F1 offspring from postnatal days 0 – 2. Several F1 weanlings (1 each at low and mid doses and 18 at the high dose) died or were euthanized prior to P2 selection. In addition, body weight was significantly decreased for F1 males at the high dose on postnatal days 0 and 1. A NOAEL of 500 mg/kg/day (LOAEL = 1,000 mg/kg/day) for offspring toxicity was identified in ECHA based on reduced body weights and increased mortality (Report date 1992).
  - In the one-generation drinking water toxicity study described above, a statistically significant increase in the total number of pre-implantation loses and a slight but not statistically significant decrease in mean litter and mean fetal weights were observed at 2.0%. A 40% incidence of whole body edema was found in fetuses in three of the eight litters at the high dose but there were no macroscopic abnormalities of the viscera in these fetuses. A statistically significant decrease in postnatal survival and average pup weight were found at the high dose. In the F1 generation, significant increase in relative liver weight was found at all dose levels, and significant increase in relative kidney weight was found at the high dose only. There was also a slight but statistically significant increase in absolute brain weight and relative empty cecum weight in both sexes at the high dose (Report date 2008).
  - A GLP-compliant developmental toxicity study was conducted according to OECD guideline 414. Pregnant New Zealand White rabbits (15/dose) received isopropanol via gavage during gestational day 6 to 18 at 0, 120, 240 or 480 mg/kg/day. There was significant maternal toxicity at the high dose demonstrated as mortality, reduced body weight gain, reduced food consumption and severe clinical signs of toxicity. Only transient, relatively mild, and nonspecific clinical signs of toxicity were found at lower doses. No developmental toxicity was observed. The authors established a developmental NOAEL at 480 mg/kg/day (Report date: 1990).

  - A second GLP-compliant developmental toxicity study was identified that was conducted according to OECD guideline 414. Pregnant Sprague-Dawley rats (25/dose) received isopropanol at 400, 800 or 1,200 mg/kg/day via daily gavage during gestational days 6 and 15. Signs of maternal toxicity were found at 800 and 1,200 mg/kg, including mortality and reduced maternal weight gain. Fetal body weight/litter was significantly reduced at 800 and 1,200 mg/kg/day. The authors identified a developmental NOAEL and LOAEL at 400 and 800 mg/kg/day, respectively (Report date 1990).
  - A third GLP-compliant developmental toxicity was conducted according to OECD guideline 414. Pregnant Wistar rats (20/dose) received isopropanol in drinking water at 0, 0.5, 1.25 or 2.5% during gestational days 6 and 16. Maternal toxicity was found at doses higher than 0.5%, demonstrated by reduced food and water consumption and body weight. There was a slight dose-dependent decrease in mean litter weight and a statistically significant reduction in mean fetal weight at doses higher than 0.5%. There was a statistically significant increase in skeletal variations that suggested a lower degree of ossification in treated animals. There were a dose-dependent decrease in the number of fetuses with the 4^{th} sacral arch and an increase in the number of fetuses with less than 2 caudal arches. Increased number of fetuses with small, absent or incompletely ossified sternebrae was also observed. A reduction in skull ossification was only observed at the low dose. There were more fetuses with forelimb proximal phalanges, less than 3 metacarpals or unilateral sternebrae at the mid dose. Increased numbers of fetuses with dumbbell shaped sternebrae or 14 pairs of ribs were found at the low and mid doses. ECHA established a NOAEL at 0.5% (equivalent to 596 mg/kg according to ECHA) for maternal and developmental toxicity, based on reduced maternal food and water consumption and decreased body weight, and decreased mean fetal body weight (Report date 2008).
- UNEP 1997
  - Available developmental toxicity studies found developmental toxicity in rats but not rabbits. In rats, developmental toxicity (decreased fetal body weight) was found at maternally toxic doses. It appears that isopropanol is not a selective developmental toxicant.
- Based on the weight of evidence, developmental toxicity consisted of mortality, decreased body weight and/or delayed ossification was found in rats at high doses that are maternally toxic. Data suggest that developmental toxicity is secondary to maternal toxicity. However, the possibility cannot be completely ruled out that isopropanol induces developmental toxicity through a mechanism independent of maternal toxicity. Therefore, ToxServices conservatively classify isopropanol to GHS category 2 (Suspected toxicant, based on some evidence from humans or experimental animals of an adverse effect on development in the absence of other toxic effects, or if occurring together with other toxic effects the adverse effect is not considered to be a secondary non-specific consequence of other toxic effects).

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

Isopropanol was assigned a score of data gap for endocrine disruption based on lack of data.

- Authoritative and Screening Lists
  - Not present on any authoritative or screening lists.
- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- Not listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.

- No data were identified.

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

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

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

Isopropanol was assigned a score of Low for acute toxicity based on oral LD_{50} greater than or equal to 3,600 mg/kg, inhalation LC_{50} equal to 39 mg/L/8h, and dermal LD_{50} equal to 12,800 mg/kg. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral and dermal LD_{50} greater than 2,000 mg/kg and 4h inhalation LC_{50} (vapor) greater than 20 mg/L(CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not on any authoritative lists.
  - *Screening:* GHS-Japan: Acute dermal toxicity category 5
  - *Screening:* GHS-Japan: Acute oral toxicity category 5
  - *Screening:* GHS-New Zealand: 6.1E (oral) – Acutely toxic (GHS category 5)
- ChemIDplus 2014
  - Oral LD_{50} = 3,600 mg/kg in mice
  - Oral LD_{50} = 6.410 mg/kg in rabbits
  - Oral LD_{50} = 5,045 mg/kg in rats
  - Dermal LD_{50} = 12,800 mg/kg in rabbits
  - Inhalation 8h LC_{50} = 16,000 ppm (= 39 mg/L[4]) in rats

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)

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

Isopropanol was assigned a score of Very High for systemic toxicity (single dose) based on classification to GHS category 1 based on human evidence. GreenScreen® criteria classify chemicals as a Very High hazard for systemic toxicity (single dose) when classified to GHS category 1(CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists.
  - *Screening:* GHS-Japan: Systemic toxicity following single exposure category 1 (based on effects on central nervous system, kidneys, and systemic toxicity)
- HSDB 2012
  - In humans, signs of acute toxicity after inhalation, ingestion or skin absorption of isopropanol include vomiting, abdominal pain, hematemesis, depressed respirations and oliguria followed by diuresis. Generalized tenderness, induration and edema of muscles may also occur. In addition, cardiovascular system effects include tachycardia and hypotension associated as the result of peripheral vasodilation. Cases of acute tubular necrosis, hepatic dysfunction, hemolytic anemia, myoglobinuria and mild hypothermia have also been reported.
- UNEP 1997
  - In humans, symptoms of acute exposure to isopropanol usually reside in the absence of

[4] 16,000 ppm is equivalent to 16,000 x MW/24,450 (mg/L) = 16,000 x 60/24,450 (mg/L) = 39 mg/L

shock.

- Based on the weight of evidence, isopropanol produced significant toxicity in humans upon large dose acute exposure. Reliable human evidence classifies isopropanol to GHS category 1

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

Isopropanol was assigned a score of Low for systemic toxicity (repeated dose) based on oral LOAELs greater than 600 mg/kg/day and inhalation LOECs greater than or equal to 4.4 mg/L/6h/day. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when oral effect levels are greater than 100 mg/kg/day and inhalation effect levels greater than 1.0 mg/L/6h/day (vapor) (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not on any authoritative lists.
  - *Screening:* GHS-Japan: Systemic toxicity following repeated exposure category 2
- ECHA 2014
  - In a GLP-compliant subchronic inhalation toxicity study conducted according to OECD guideline 413, F344 rats (10/sex/dose at 100 ppm and 25/sex/dose for the other groups) and CD-1 mice (10/sex/dose) were exposed to isopropanol via whole-body inhalation at 0, 100, 500, 1,500 or 5,000 ppm for 6 hours/day, 5 days/week for 13 weeks (equivalent to 0, 0.18, 0.88, 2.6 and 8.8 mg/L/6h/day[5]). In rats, there were decreased absolute body weight and body weight gain and changes in hematology parameters (suggestive of a transient slight anemia) at 1,500 and 5,000 ppm. Relative liver weight was increased in both sexes at 5,000 ppm. Histological examination revealed hyaline droplets in the kidneys of all male rats including controls, with a non-dose-related increase in size and frequency of these droplets. The biological significance of this kidney pathology is unclear. In mice, increased body weight and body weight gain were observed at 5,000 ppm in females only. Changes in hematology were observed in female mice at 5,000 ppm, indicative of a slight dehydration effect. Increased relative liver weight was found in female mice at 5,000 ppm. No other effects were noted. ToxServices established the NOAEL and LOAEL of 1,500 (2.6 mg/L/6h/day) and 5,000 ppm (8.8 mg/L/6h/day), respectively, based on changes in body weight and liver weight, and in hematology parameters (Report date 1991).
  - A GLP-compliant combined repeated dose and carcinogenicity study was conducted according to OECD guideline 451. Fisher 344 rats (65/sex/dose for the core group and 10/sex/dose for interim sacrifice) were exposed to isopropanol via whole body inhalation at 0, 500, 2,500 or 5,000 ppm for 6 hours/day, 5 days/week for 104 weeks (equivalent to 0, 0.88, 4.4, and 8.8 mg/L/6h/day[6]). Changes in body weight and urinalysis parameters indicative of kidney changes (decrease in osmolality and increase in total volume and/or protein) were found at 2,500 and 5,000 ppm. Increased absolute and relative kidney weight was observed in males at 2,500 ppm and in females at 5,000 ppm. There were macroscopic changes such as granular kidney in males and females at the mid and high concentrations. Microscopically, a number of lesions were reported, with the most significant being in the kidney (details not provided for males). In females, there was increased severity of glomerulosclerosis and increased renal disease at the highest concentration. ECHA considered the kidney effects species-specific and not adverse,

[5] 100 ppm is equivalent to 100 x MW/24,450 (mg/L) = 100 x 60/24,450 mg/L = 0.245 mg/L. Treatment frequency adjustment: 0.245 mg/L x 5/7 = 0.18 mg/L/6h/day

[6] 500 ppm is equivalent to 500 x MW/24,450 (mg/L) = 500 x 60/24,450 mg/L = 1.23 mg/L. Treatment frequency adjustment: 1.23 mg/L x 5/7 = 0.88 mg/L/6h/day

and established the NOAEC at 5,000 ppm for systemic toxicity. Although it appears that the kidney lesions (hyaline droplets) in male rats may be associated with the $\alpha_{2\mu}$-globulin mechanism that is specific to male rats and not relevant to humans, kidney effects were also observed in female rats, including changed kidney weight, increased severity of glomerulosclerosis and renal disease. With limited details provided in this study, ToxServices established the LOAEL at 5,000 ppm (8.8 mg/L/6h/day) based on kidney effects in female rats (Burleigh-Flayer H et al. 1997 as cited in ECHA 2014).

- A GLP-compliant combined repeated dose and carcinogenicity study was conducted according to OECD guideline 451. CD-1 mice (55/sex/dose for the core group and 10/sex/dose for interim sacrifice) were exposed to isopropanol via whole body inhalation at 0, 500, 2,500 or 5,000 ppm for 6 hours/day, 5 days/week for 78 weeks (equivalent to 0, 0.88, 4.4, and 8.8 mg/L/6h/day[7]). A concentration-related increase in body weight and body weight gain was reported for male mice, with statistical significance reached at 2,500 and 5,000 ppm. There was a concentration related increase in absolute and relative liver weight in female mice that reached statistical significance at 5,000 ppm. ECHA established a NOEC at 500 ppm (0.88 mg/L/6h/day) and LOEC at 2,500 ppm (4.4 mg/L/6h/day) based on increased body weight and body weight gain (Burleigh-Flayer H et al. 1997 as cited in ECHA 2014).
- A GLP-compliant range finding study for a 14 week study equivalent to OECD guideline 412 was identified, but was not described here as the exposure duration was only 9 days.

- UNEP 1997
  - A few additional repeated dose toxicity studies were identified through oral (two subchronic oral toxicity studies established NOELs > 600 mg/kg/day) and inhalation routes. It was summarized that the only target organ was kidney. In rats, accumulation of hyaline droplets in proximal tubule cells (males) and an exacerbation of chronic progressive nephropathy (males and females) was found, a spontaneous disease common in aged rats (male and females) of unknown etiology. In mice, effects were minimal to mild, including renal tubular proteinosis and tubular dilation in chronic studies. There was not concentration-related increase in severity and frequency for renal tubular proteinosis, and no corresponding evidence of alterations to the glomeruli. Tubular dilation was observed in a small number of females at 2,500 and 5,000 ppm, but was statistically significant only at 5,000 ppm. This effect was not seen in males, and was not accompanied by tubular cell degeneration or urinary outflow obstruction.
- NITE 2006
  - Isopropanol was classified to GHS category 2 based on effects on blood vessel, liver and spleen in a 86-day inhalation toxicity study in rats (date: 1990). No further details were available and the study could not be located.
- Based on the weight of evidence, although the study identified in NITE (conducted prior to 1990) may potentially classify the chemical to GHS category 2, the actual study or its summary could not be found. In addition, in more recent, GLP-compliant subchronic inhalation studies in rats, no adverse effects were identified on blood vessels, liver or spleen. Therefore, this study was not considered in this evaluation. Available data suggest that the oral LOAEL in subchronic studies are > 600 mg/kg/day, and inhalation LO(A)ECs ≥ 4.4 mg/L/6h/day.

[7] 500 ppm is equivalent to 100 x MW/24,450 (mg/L) = 500 x 60/24,450 mg/L = 1.23 mg/L. Treatment frequency adjustment: 1.23 mg/L x 5/7 = 0.88 mg/L/6h/day

Neurotoxicity (N)

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

Isopropanol was assigned a score of Moderate for neurotoxicity (single dose) based on classification to GHS category 3 based on narcotic effects in humans. GreenScreen® criteria classify chemicals as a Moderate hazard for neurotoxicity (single dose) when classified to GHS category 3 (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* EU H336: May cause drowsiness or dizziness
  - *Authoritative:* EU R67: Vapor may cause drowsiness and dizziness
  - *Screening:* Grandjean & Landrigan: Known to be neurotoxic in man
  - *Screening:* Patty's Toxicology - Boyes Neurotoxicants: Neurotoxic
- HSDB 2012
  - The principal effect of acute isopropyl poisoning in humans is CNS depression, demonstrated by symptoms such as areflexia, headache, mental depression hallucinations, distorted perceptions, dizziness, poor coordination, confusion that progress to stupor and deep coma, and loss of deep tendon reflexes in serious cases. The CNS effects often persist for 24 hours. Lethality cases were reported from acute inhalation and oral exposure to isopropanol.
- Based on the weight of evidence, the typical effect from acute exposure to isopropanol is narcotic effects in humans. According to GHS criteria, human evidence of narcotic effects classifies chemicals to GHS category 3.

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

Isopropanol was assigned a score of Low for neurotoxicity (repeated dose) based on the lowest LOAEC of 8.8 mg/L/6h/day. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (repeated dose) when critical effect concentrations (vapor) are > 1 mg/L/6h/day (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* EU H336: May cause drowsiness or dizziness
  - *Authoritative:* EU R67: Vapor may cause drowsiness and dizziness
  - *Screening:* Grandjean & Landrigan: Known to be neurotoxic in man
  - *Screening:* Patty's Toxicology - Boyes Neurotoxicants: Neurotoxic
- ECHA 2014
  - In the GLP-compliant subchronic inhalation toxicity study conducted according to OECD guideline 413 as detailed previously, F344 rats (10/sex/dose at 100 ppm and 25/sex/dose for the other groups) were exposed to isopropanol via whole-body inhalation at 0, 100, 500, 1,500 or 5,000 ppm for 6 hours/day, 5 days/week for 13 weeks (equivalent to 0, 0.18, 0.88, 2.6 and 8.8 mg/L/6h/day[8]). Neurobehavioral examination was carried out, including functional observational battery (FOB) at weeks 0, 1, 2, 4, 9 and 13, and motor activity evaluations at weeks 0, 4, 9 and 13. No changes were observed regarding FOB, but an increase in motor activity was reported in females at 5,000 ppm at week 8 and 13. ToxServices established the NOAEC and LOAEC at 1,500 (2.6 mg/L/6h/day) and 5,000 ppm (8.8 mg/L/6h/day), respectively, based on increased motor activity in females (Report date 1991).
  - A GLP-compliant developmental neurotoxicity study was conducted according to OECD guideline 426. Pregnant Sprague-Dawley rats (64/dose) were exposed to isopropanol by daily oral gavage from gestation day 6 to postnatal day 21, at the dose of 0, 200, 700 or

[8] 100 ppm is equivalent to 100 x MW/24,450 (mg/L) = 100 x 60/24,450 mg/L = 0.245 mg/L. Treatment frequency adjustment: 0.245 mg/L x 5/7 = 0.18 mg/L/6h/day

1,200 mg/kg/day. Motor activity of the pups was evaluated on days 13, 17, 21, 47 and 58. Auditory startle reflex habituation was evaluated on days 22 and 60. Active avoidance test was conducted on days 60 – 64. At study termination, brain weight was measured and histopathological examination was performed on tissues from the control and high dose pups. Isopropanol did not lead to any neurotoxic effects examined. Therefore, ECHA established the NOAEL at 1,200 mg/kg/day for developmental neurotoxicity (report date 1991).

  - A GLP-compliant neurotoxicity study was conducted according to OECD guideline 413. Female Fischer 344 rats (30/group) were exposed to isopropanol via inhalation at 5,000 ppm for 6 hours/day, 5 days/week for 9 or 13 weeks. There was no mortality during the study. Clinical signs included hypoactivity and lack of a startle reflex. Decreased body weight and body weight gain were noted at the beginning of the study, but gradually improved. There was an increase in total motor activity (ambulation, fine motor activity and rearing activity) and mean cumulative motor activity (the sum of total activity across the 90-min test session). ToxServices identified the LOAEC at 5,000 ppm (8.8 mg/L/6h/day[9]).

- Based on the weight of evidence, isopropanol is not a developmental neurotoxicant. Although acute exposure led to narcosis, repeated lower dose exposure does not appear to adversely affect neurological parameters irreversibly. The lowest LOAEC was 8.8 mg/L/6h/day based on motor activity increase in female rats.

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

Isopropanol was assigned a score of Moderate for skin sensitization based on classification to GHS category 1B. GreenScreen® criteria classify chemicals as a Moderate hazard for skin sensitization when classified to GHS category 1B (CPA 2012a).

- Authoritative and Screening Lists
  - Not present on any authoritative or screening lists.
- HSDB 2012
  - Two patients with primary alcohol dermatitis and hypersensitivity tested strongly positive for sensitization to secondary alcohol isopropanol.
  - One occupationally-acquired sensitivity case to isopropanol was confirmed through patch testing.
- UNEP 1997
  - Isopropanol was found not to be dermally sensitizing in guinea pigs in a Buehler test. No further details were available (report date: 1980).
- Based on the weight of evidence, isopropanol is not likely to be a strong skin sensitizer, but rare cases in humans have been reported in humans. Therefore, ToxServices conservatively classified isopropanol to GHS category 1B (low to moderate frequency of occurrence).

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

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

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

[9] 5000 ppm is equivalent to 5000 x MW/24,450 (mg/L) = 5000 x 60/24,450 mg/L = 12.3 mg/L. Treatment frequency adjustment: 12.3 mg/L x 5/7 = 8.8 mg/L/6h/day

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M, or L): M
Isopropanol was assigned a score of Moderate for skin irritation/corrosivity based on classification to GHS category 3. GreenScreen® criteria classify chemicals as a Moderate hazard for skin irritation/corrosivity when they are classified to GHS category 3 (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not on any authoritative lists.
  - *Screening:* GHS-New Zealand: 6.3B – Mildly irritating to the skin (Category 3)
- UNEP 1997
  - Isopropanol produced little irritation on the skin of volunteers, although isolated cases of dermal irritation were reported.
  - A non-GLP study reported lack of irritation potential in rabbits (report date: 1975).
- RTECS 2013
  - Administration of 500 mg isopropanol on the rabbit skin led to a mild irritating effect.
- Based on the weight of evidence, isopropanol is at most a mild skin irritant, classifying it to GHS category 3 (mild irritant).

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M, or L): H
Isopropanol was assigned a score of High for eye irritation/corrosivity based on data in animals and on association with EU H319. GreenScreen® criteria classify chemicals as a High hazard for eye irritation/corrosivity when they are classified to GHS category 2A as irritating to the eyes and/or are associated with EU H319 (CPA 2012a).

- Authoritative and Screening Lists
  - Authoritative: EU H319: Causes serious eye irritation
  - *Screening:* GHS-New Zealand: 6.4A – Irritating to the eye
  - *Screening:* GHS-Japan: Serious eye damage category 2
- HSDB 2012
  - Isopropanol vapor is mildly irritating to the human eyes.
- UNEP 1997
  - Isopropanol was determined to be moderately irritating to irritating in four Draize tests to the eyes of rabbits conducted in 1973-1987.

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): L
Isopropanol was assigned a score of Low for acute aquatic toxicity based on acute aquatic L/EC_{50} values of greater than 1,000 mg/L in fish, aquatic invertebrates and green algae. GreenScreen® criteria classify chemicals as a Low hazard for acute aquatic toxicity when acute aquatic L/EC_{50} values are greater than 100 mg/L in fish, aquatic invertebrates and green algae (CPA 2012a).

- Authoritative and Screening Lists
  - Not present on any authoritative or screening lists.
- UNEP 1997
  - 96h LC_{50} = 9,640 mg/L in fathead minnow
  - 24h EC_{50} > 10,000 mg/L in daphnia
  - 48h LC_{50} = 1,400 mg/L in cragon (aquatic invertebrate)
  - Toxicity threshold = 1,800 mg/L in green algae

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

Isopropanol was assigned a score of Low for chronic aquatic toxicity based on 16-21 day NOEC of > 10 mg/L in daphnia, supported by predicted ChV of greater than 10 mg/L in fish, daphnia and algae. GreenScreen® criteria classify chemicals as a Low hazard for chronic aquatic toxicity when chronic values are greater than 10 mg/L (CPA 2012a).

- Authoritative and Screening Lists
  - Not present on any authoritative or screening lists.
- UNEP 1997
  - 16 day NOEC = 141 mg/L in daphnia
  - 21 day NOEC = 30 mg/L in daphnia
- U.S. EPA 2012b
  - ChV = 141 mg/L in fish
  - ChV = 53 mg/L in daphnia
  - ChV = 60 mg/L in green algae (Appendix D)

Environmental Fate (Fate)

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

Isopropanol was assigned a score of Very Low for persistence based on being readily biodegradable meeting the 10 day window in multiple tests. GreenScreen® criteria classify chemicals as a Very Low hazard for persistence when they meet the 10-day window in "ready biodegradation test" (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* There are no authoritative lists for this endpoint
  - *Screening:* Environment Canada DSL: Persistent
- UNEP 1997
  - Biodegradation was 49% after 5 days in a BOD test, under non-acclimated conditions.
  - Isopropanol was readily biodegradable in both freshwater and saltwater media with 72 – 78% biodegradation in 20 days.
- HSDB 2012
  - In municipal waste water, isopropanol was biodegraded 7% and 70% after 5 and 20 days, respectively, as measured by theoretical oxygen demand (ThOD). When 3, 7 and 10 mg/L isopropanol was added to fresh water with filtered sewage seed, 28% and 78% degradation were reached after 5 and 20 days. When the same concentrations of isopropanol were tested using filtered sewage seed in salt water, ThOD of 13% and 72% was measured in 5 and 20 days, respectively.
  - Two studies reported 66% and 74% biodegradation in domestic waste water after 5 days.
  - Up to 99% biodegradation was reached when using acclimated activated sludge in the system at 20ºC.
  - Filtered sewage seed and acclimated sewage seed resulted in 49% and 72% biodegradation (ThOD) after 5 days, respectively.
  - 58% degradation was achieved in 5 days with sewage at 20ºC
  - 13% and 72% biodegradation were achieved in 5 and 20 days, respectively, in domestic waste water diluted with salt water.
  - In a Japanese MITI test, isopropanol was determined to be readily biodegradable, reaching 86% of theoretical BOD in 2 weeks with an activated sludge inoculum at 30 mg/L.

- U.S. EPA 2012a
    - The BIOWIN modeling Ready Biodegradable Predictor (Appendix E) indicates that isopropanol is expected to be readily biodegradable. Fugacity modeling predicts 50.1% will partition to soil with a half-life of 30 days, 45.2% will partition to water with a half-life of 15 days, and 4.586% will partition to air with a half-life of 2.1 days.
- Based on the weight of evidence, isopropanol is readily biodegradable in water and a score of Very Low was assigned. Fugacity modeling predicts that isopropanol was readily biodegradable and it met the 10-day window in multiple tests. When the major compartment is soil, GreenScreen® criteria specify a score of Very Low if the chemical meets the 10-day window in a ready biodegradation test. It is not clear why Environment Canada classified it as persistent.

Bioaccumulation (B) Score (vH, H, M, L, or vL): vL
Isopropanol was assigned a score of Very Low for bioaccumulation based on predicted BCF of 0.9639 and a measured log K_{ow} of 0.05. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when BCF/BAF is less than or equal to 100 and/or log K_{ow} is less than or equal to 4 (CPA 2012a).

- Authoritative and Screening Lists
    - Not present on any authoritative or screening lists.
- HSDB 2012
    - A BCF of 3 was calculated for isopropanol based on a log K_{ow} of 0.05, using the U.S. EPA's EPI Suite version 4.1. This indicates that this chemical has a low bioconcentration potential.
- U.S. EPA 2012a
    - BCFBAF estimated a BCF of 0.9639 for isopropanol based on a log K_{ow} of 0.05 (Appendix E).

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): *H*
Isopropanol was assigned a score of High for reactivity based on classification to GHS explosives category 1.3. GreenScreen® criteria classify chemicals as a High hazard for reactivity when classified to GHS category 1.1, 1.2 or 1.3 for explosives (CPA 2012a).

- Authoritative and Screening Lists
    - Not on any authoritative or screening lists.
- HSDB 2012
    - Moderately explosive when exposed to heat or flame.
    - Isopropanol can form unstable peroxides after prolonged contact with air, and the concentrated air-isopropanol mixture can explode during distillation/evaporation.
    - NFPA hazard classification: Instability = 0: materials that are normally stable, even under fire exposure conditions, and that do not react with water.
- UNEP 1997
    - Isopropanol vapor can form an explosive mixture with air at room temperature. It does not have any oxidizing properties.
- Based on the weight of evidence, isopropanol may have a moderate explosion hazard upon heating. As no measured data can be obtained, an accurate GHS classification is not possible. Based on qualitative information listed above, ToxServices classified isopropanol to GHS explosives category 1.3: substances with a fire hazard and either a minor blast hazard or a minor projection hazard or both, but not a mass explosion hazard: (i) Combustion of which gives rise to

considerable radiant heat; or (ii) which burn one after another, producing minor blast or projection effects or both.

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

Isopropanol was assigned a score of High for flammability based on classification to GHS flammable liquid category 2, and on association with EU R225 and DOT class 3 group 2. GreenScreen® criteria classify chemicals as a High hazard for flammability when classified to GHS category 2 as flammable liquids, and/or are associated with EU H225 and or DOT class 3 group 2 (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* EU H225: Highly flammable liquid and vapor
  - *Authoritative:* EU R11: Highly flammable
  - *Authoritative:* WHMIS: Class B2 – Flammable liquids
  - *Authoritative:* DOT: Class 3 group II flammable liquids
  - *Screening:* Not on any screening lists.
- HSDB 2012
  - Flash point = 12ºC
  - Boiling point = 82.3ºC at 760 mmHg
- Based on the weight of evidence, isopropanol is classified to GHS category 2 as a flammable liquid (flashpoint less than 23ºC and initial boiling point greater than 35ºC)

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APPENDIX A: Hazard Benchmark Acronyms
(in alphabetical order)

(AA) Acute Aquatic Toxicity

(AT) Acute Mammalian Toxicity

(B) Bioaccumulation

(C) Carcinogenicity

(CA) Chronic Aquatic Toxicity

(Cr) Corrosion/ Irritation (Skin/ Eye)

(D) Developmental Toxicity

(E) Endocrine Activity

(F) Flammability

(IrE) Eye Irritation/Corrosivity

(IrS) Skin Irritation/Corrosivity

(M) Mutagenicity and Genotoxicity

(N) Neurotoxicity

(P) Persistence

(R) Reproductive Toxicity

(Rx) Reactivity

(SnS) Sensitization- Skin

(SnR) Sensitization- Respiratory

(ST) Systemic/Organ Toxicity

APPENDIX B: Results of Automated GreenScreen® Score Calculation for Isopropanol (CAS #67-63-0)

TOXSERVICES TOXICOLOGY RISK ASSESSMENT CONSULTING

GREEN SCREEN FOR SAFER CHEMICALS

GreenScreen® Score Inspector

Table 1: Hazard Table

			Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
			Carcinogenicity	Mutagenicity/Genotoxicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
Table 2: Chemical Details									S	R *	S	R *	*	*								
Inorganic Chemical?	Chemical Name	CAS#	C	M	R	D	E	AT	STs	STr	Ns	Nr	SNS*	SNR*	IrS	IrE	AA	CA	P	B	Rx	F
No	Isorpropanol	67-63-0	L	L	M	M	DG	L	vH	L	M	L	*M*	DG	M	H	L	L	vL	vL	H	H

Table 3: Hazard Summary Table

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

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Isorpropanol	2

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

Table 6

Chemical Name	Final GreenScreen® Benchmark Score
Isorpropanol	2

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

Table 5: Data Gap Assessment Table

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

APPENDIX C: Pharos Output for Isopropanol (CAS #67-63-0)

Isopropyl Alcohol

CAS RN: 67-63-0

Synonyms: 2-propanol, isopropanol, rubbing alcohol, iPrOH

Detailed Direct Hazard Listings — Quickscreen

REPRODUCTIVE	Japan METI/MOE - GHS Classifications (GHS-Japan) Toxic to reproduction - Category 2 - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Specific target organs/systemic toxicity following single exposure - Category 1 - GreenScreen Benchmark Unspecified (LT-U)
FLAMMABLE	EC - CLP/GHS Hazard Statements (EU H-Statements) H225 Highly flammable liquid and vapour. - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only - HPD
FLAMMABLE	New Zealand HSNO/GHS (GHS-New Zealand) 3.1B - Flammable Liquids: high hazard - GreenScreen Benchmark Unspecified (LT-U)
FLAMMABLE	Japan METI/MOE - GHS Classifications (GHS-Japan) Flammable liquids - Category 2 - GreenScreen Benchmark Unspecified (LT-U)
CANCER	Intnl Agency for Rsrch on Cancer - Cancer Monographs (IARC) Group 3: Agent is not classifiable as to its carcinogenicity to humans - GreenScreen Benchmark Unspecified (LT-U)
DEVELOPMENTAL	German MAK - List of Substances (MAK) Pregnancy Risk Group C - GreenScreen Benchmark Unspecified (LT-U)
NEUROTOXICITY	Lancet - Grandjean & Landrigan Neurotoxic Chemicals (G&L Neuro) Known to be neurotoxic in man - GreenScreen Benchmark Unspecified (LT-U)
NEUROTOXICITY	EC - CLP/GHS Hazard Statements (EU H-Statements) H336 May cause drowsiness or dizziness - GreenScreen Benchmark Unspecified (LT-U)
NEUROTOXICITY	Pattys Toxicology - Boyes Neurotoxicants (Boyes-N) Neurotoxic - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Québec CSST - WHMIS Classifications (WHMIS) Class D2B - Toxic material causing other toxic effects - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Acute toxicity (dermal) - Category 5 - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Acute toxicity (oral) - Category 5 - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Specific target organs/systemic toxicity following repeated exposure - Category 2 - GreenScreen Benchmark Unspecified (LT-U)
EYE IRRITATION	EC - Risk Phrases (EU R-Phrases) R36: Irritating to eyes. - GreenScreen Benchmark Unspecified (LT-U) - HPD
EYE IRRITATION	EC - CLP/GHS Hazard Statements (EU H-Statements)

EYE IRRITATION	H319 Causes serious eye irritation - GreenScreen Benchmark Unspecified (LT-U) - HPD
EYE IRRITATION	New Zealand HSNO/GHS (GHS-New Zealand) 6.4A - Irritating to the eye - GreenScreen Benchmark Unspecified (LT-U)
EYE IRRITATION	Japan METI/MOE - GHS Classifications (GHS-Japan) Serious eye damage / eye irritation - Category 2 - GreenScreen Benchmark Unspecified (LT-U)
SKIN IRRITATION	New Zealand HSNO/GHS (GHS-New Zealand) 6.3B - Mildly irritating to the skin - GreenScreen Benchmark Unspecified (LT-U)
FLAMMABLE	Québec CSST - WHMIS Classifications (WHMIS) Class B2 - Flammable liquids - GreenScreen Benchmark Unspecified (LT-U)
PBT	Environment Canada - Domestic Substances List (DSL) DSL substances that are Persistent - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	New Zealand HSNO/GHS (GHS-New Zealand) 6.1E (oral) - Acutely toxic - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Japan METI/MOE - GHS Classifications (GHS-Japan) Aspiration hazard - Category 2 - Not included in GreenScreen - occupational hazard only
RESTRICTED LIST	German FEA - Substances Hazardous to Waters (VwVwS) Class 1 Low Hazard to Waters - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only
RESTRICTED LIST	CA SCP Candidate Chemicals Full Candidate Chemical List - Not included in GreenScreen

Lifecycle Hazard Quickscreen

Full Lifecycle Map

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

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

ACUTE AQUATIC	ZINC OXIDE [1314-13-2] - Occasional/Rare Catalyst
CHRON AQUATIC	ZINC OXIDE [1314-13-2] - Occasional/Rare Catalyst

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

PBT	SULFURIC ACID [7664-93-9] - Frequent Additive - Reactive
CANCER	SULFURIC ACID [7664-93-9] - Frequent Additive - Reactive
DEVELOPMENTAL	SULFURIC ACID [7664-93-9] - Frequent Additive - Reactive
RESPIRATORY	SULFURIC ACID [7664-93-9] - Frequent Additive - Reactive
NEUROTOXICITY	PHOSPHORIC ACID [7664-38-2] - Frequent Intermediate
MAMMALIAN	SULFURIC ACID [7664-93-9] - Frequent Additive - Reactive
EYE IRRITATION	SULFURIC ACID [7664-93-9] - Frequent Additive - Reactive
SKIN IRRITATION	SULFURIC ACID [7664-93-9] - Frequent Additive - Reactive
TERRESTRIAL	Tungsten trioxide [1314-35-8] - Occasional/Rare Intermediate
FLAMMABLE	PROPYLENE [115-07-1] - Frequent Feedstock
REACTIVE	SULFURIC ACID [7664-93-9] - Frequent Additive - Reactive
RESTRICTED LIST	PROPYLENE [115-07-1] - Frequent Feedstock

APPENDIX D: ECOSAR Modeling Results for Isopropanol (CAS #67-63-0)

ECOSAR Version 1.11 Results Page

SMILES: OC(C)C
CHEM: 2-Propanol
CAS Num: 000067-63-0
ChemID1:
MOL FOR: C3 H8 O1
MOL WT: 60.10
Log K_{ow}: 0.276 (EPISuite K_{ow}win v1.68 Estimate)
Log K_{ow}: (User Entered)
Log K_{ow}: 0.05 (PhysProp DB exp value - for comparison only)
Melt Pt: (User Entered for Wat Sol estimate)
Melt Pt: -89.50 (deg C, PhysProp DB exp value for Wat Sol est)
Wat Sol: 4.562E+005 (mg/L, EPISuite WSK_{ow}win v1.43 Estimate)
Wat Sol: (User Entered)
Wat Sol: 1E+006 (mg/L, PhysProp DB exp value)

Values used to Generate ECOSAR Profile

Log K_{ow}: 0.276 (EPISuite K_{ow}win v1.68 Estimate)
Wat Sol: 1E+006 (mg/L, PhysProp DB exp value)

Available Measured Data from ECOSAR Training Set

CAS No	Organism	Duration	End Pt	Measured mg/L (ppm)	Ecosar Class	Reference
000067-63-0	Fish	96-hr	LC50	6550	Neutral organics	DUL
000067-63-0	Fish	96-hr	LC50	9640	Neutral organics	DUL
000067-63-0	Fish	96-hr	LC50	10400	Neutral organics	DUL

ECOSAR v1.1 Class-specific Estimations

Neutral Organics

ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
Neutral Organics	: Fish	96-hr	LC50	1743.475
Neutral Organics	: Daphnid	48-hr	LC50	844.305
Neutral Organics	: Green Algae	96-hr	EC50	325.707
Neutral Organics	: Fish		ChV	141.250
Neutral Organics	: Daphnid		ChV	52.874

Neutral Organics	: Green Algae		ChV	59.842
Neutral Organics	: Fish (SW)	96-hr	LC50	2172.373
Neutral Organics	: Mysid	96-hr	LC50	5189.405
Neutral Organics	: Fish (SW)		ChV	82.307
Neutral Organics	: Mysid (SW)		ChV	747.558
Neutral Organics	: Earthworm	14-day	LC50	157.684

Note: * = asterisk designates: Chemical may not be soluble enough to measure this predicted effect. If the effect level exceeds the water solubility by 10X, typically no effects at saturation (NES) are reported.

Class Specific LogK_{ow} Cut-Offs

If the log K_{ow} of the chemical is greater than the endpoint specific cut-offs presented below, then no effects at saturation are expected for those endpoints.

Neutral Organics:

Maximum LogK_{ow}: 5.0 (Fish 96-hr LC50; Daphnid LC50, Mysid LC50)
Maximum LogK_{ow}: 6.0 (Earthworm LC50)
Maximum LogK_{ow}: 6.4 (Green Algae EC50)
Maximum LogK_{ow}: 8.0 (ChV)

APPENDIX E: EPISuite Modeling Results for Isopropanol (CAS #67-63-0)

CAS Number: 67-63-0
SMILES: OC(C)C
CHEM: 2-Propanol
MOL FOR: C3 H8 O1
MOL WT: 60.10
---------- EPI SUMMARY (v4.11) ----------

Physical Property Inputs:
Log K_{ow} (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 K_{ow} (KOWWIN v1.68 estimate) = 0.28
Log K_{ow} (Exper. database match) = 0.05
Exper. Ref: HANSCH, C. ET AL. (1995)

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 66.97 (Adapted Stein & Brown method)
Melting Pt (deg C): -89.16 (Mean or Weighted MP)
VP(mm Hg, 25 deg C): 49.6 (Mean VP of Antoine & Grain methods)
VP (Pa, 25 deg C): 6.61E+003 (Mean VP of Antoine & Grain methods)
MP (exp database): -89.5 deg C
BP (exp database): 82.3 deg C
VP (exp database): 4.54E+01 mm Hg (6.05E+003 Pa) at 25 deg C

Water Solubility Estimate from Log K_{ow} (WSKOW v1.42):
Water Solubility at 25 deg C (mg/L): 4.024e+005
log K_{ow} used: 0.05 (expk_{ow} database)
no-melting pt equation used
Water Sol (Exper. database match) = 1e+006 mg/L (25 deg C)
Exper. Ref: RIDDICK, J.A ET AL. (1986)

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 2.8724e+005 mg/L

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

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method: 7.52E-006 atm-m3/mole (7.62E-001 Pa-m3/mole)
Group Method: 1.14E-005 atm-m3/mole (1.16E+000 Pa-m3/mole)
Exper. Database: 8.10E-06 atm-m3/mole (8.21E-001 Pa-m3/mole)
For Henry LC Comparison Purposes:

User-Entered Henry LC: not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC: 9.747E-006 atm-m3/mole (9.876E-001 Pa-m3/mole)
VP: 49.6 mm Hg (source: MPBPVP)
WS: 4.02E+005 mg/L (source: WSKOWWIN)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
Log K_{ow} used: 0.05 (exp database)
Log K_{aw} used: -3.480 (exp database)
Log Koa (KOAWIN v1.10 estimate): 3.530
Log Koa (experimental database): 3.410

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model): 0.8777
Biowin2 (Non-Linear Model): 0.9635
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 3.2263 (weeks)
Biowin4 (Primary Survey Model): 3.8905 (days)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model): 0.6446
Biowin6 (MITI Non-Linear Model): 0.8499
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): 0.6439
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): 6.05E+003 Pa (45.4 mm Hg)
Log Koa (Exp database): 3.410
Kp (particle/gas partition coef. (m^3/µg)):
Mackay model : 4.96E-010
Octanol/air (Koa) model: 6.31E-010
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model : 1.79E-008
Mackay model : 3.96E-008
Octanol/air (Koa) model: 5.05E-008

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 7.2646 E-12 cm3/molecule-sec
Half-Life = 1.472 Days (12-hr day; 1.5E6 OH/cm3)
Half-Life = 17.668 Hrs.
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
2.88E-008 (Junge-Pankow, Mackay avg)
5.05E-008 (Koa method)

Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (K_{oc}WIN v2.00):
K_{oc}: 1.53 L/kg (MCI method)
Log K_{oc}: 0.185 (MCI method)
K_{oc}: 3.478 L/kg (K_{ow} method)
Log K_{oc}: 0.541 (K_{ow} method)

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

Bioaccumulation Estimates (BCFBAF v3.01):
Log BCF from regression-based method = 0.500 (BCF = 3.162 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -1.4384 days (HL = 0.03644 days)
Log BCF Arnot-Gobas method (upper trophic) = -0.016 (BCF = 0.9639)
Log BAF Arnot-Gobas method (upper trophic) = -0.016 (BAF = 0.9639)
log K_{ow} used: 0.05 (expk_{ow} database)

Volatilization from Water:
Henry LC: 8.1E-006 atm-m3/mole (Henry experimental database)
Half-Life from Model River: 56.83 hours (2.368 days)
Half-Life from Model Lake: 684.9 hours (28.54 days)

Removal In Wastewater Treatment:
Total removal: 2.30 percent
Total biodegradation: 0.09 percent
Total sludge adsorption: 1.75 percent
Total to Air: 0.45 percent
(using 10000 hr Bio P,A,S)

Removal In Wastewater Treatment:
Total removal: 92.07 percent
Total biodegradation: 91.66 percent
Total sludge adsorption: 0.34 percent
Total to Air: 0.08 percent
(using Biowin/EPA draft method)

Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	4.58	50.6	1000
Water	45.2	360	1000
Soil	50.1	720	1000
Sediment	0.0856	3.24e+003	0

Persistence Time: 346 hr

Authorized Reviewers

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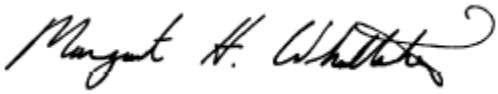

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