Green Screen Assessment Prepared By:
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Organization: PNW Pollution Prevention Resource Center
Date: 30 June 2012

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Date: April 22, 2013

GreenScreen™ Assessment for Acetone (CAS # 67-64-1)

GreenScreen™ Version 1.2 Draft Assessment
Note: Validation Has Not Been Performed on this Green Screen Assessment

Chemical Name: Acetone

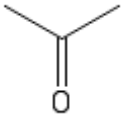
Confirm application of the de minimus rule[1]: (if no, what *de minimus* did you use?) Yes.

Chemical Name (CAS #): Acetone (CAS# 67-64-1)

Also called: 2-propanone, methyl ketone, beta-ketopropane, propan-2-one, pyroacetic acid.

Chemical Surrogates, analogs or moieties used in this assessment (CAS #s): Isopropanol (propan-2-ol) CAS # 67-63-0

Chemical Structure(s):



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

1. Chemical intermediate for methyl methacrylate, methacrylic acid and higher methacrylates, methyl isobutyl ketone, bisphenol a, acetic acid (ketene process), diacetone alcohol, chloroform, iodoform, bromoform, explosives, etc.
2. Solvent for fats, oils, waxes, resins, rubber, plastics, lacquers, varnishes (including nail polish), adhesives, printing inks and cements; cleaning and drying parts of all kinds. Extraction solvent for various plant and animal products.
3. Processing aid for manufacture of cellulose acetate.

See Background section below for references.

GreenScreen Rating[2]: Acetone was assigned a **Benchmark Score of 2** based on:

- Did not fail any Benchmark 1 criteria.
- Failed Benchmark 2c (very high persistence and moderate neurotoxicity) and 2g (high flammability).

GreenScreen Hazard Ratings: Acetone																			
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	repeat*	single	repeat*										
L	**L**	*L*	*L*	DG	**L**	**L**	**L**	**M**	*M*	**L**	DG	**L**	**H**	**L**	**L**	*vH*	**vL**	**L**	**H**

Note: Hazard levels [Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)] in *italics* reflect estimated values and lower confidence. Hazard levels in **BOLD** font reflect values based on test data (See Guidance). NE indicates no determination was made (conflicting data); DG indicates insufficient data for assigning a hazard level.

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

[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.

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Transformation Products and Ratings:

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

Functional Use	Life Cycle Stage	Transformation Pathway	Transformation Products	CAS #	On CPA Red List[4]?	Green Screen Rating[5]
N/A						

No fate or transformation products relevant to toxicity were identified.

Background

Acetone is a clear colorless liquid. It is highly flammable and very soluble with water. Acetone is used as a solvent for fats, oils, waxes, resins, rubber, plastics, lacquers, varnishes, and rubber cements and is a major component of nail polish remover. Acetone is used as a chemical intermediate in the synthesis of a wide range of substances, including chloroform, ketene, acetic acid, iodoform, mesityl oxide, tribromomethane, explosives, diacetone alcohol, rayon, methyl methacrylate, bisphenol A, methyl isobutyl ketone, etc. (NTP 1991).

Large-scale commercial production of acetone is generally accomplished by one of two processes. The most common process employs the acid catalyzed hydrolytic cleavage of cumene hydroperoxide. Acetone and phenol are co-products in this reaction. Catalytic dehydrogenation of isopropyl alcohol accounted for about 6% of US acetone production in 1995. Other production methods include fermentation, propylene oxidation, and diisopropyl-benzene oxidation, but these account for only a small percentage of production (UNEP 1999).

Acetone is hygroscopic and reagent grade acetone can contain up to 0.5% water as well as small amounts of other polar solvents. Major impurity compounds identified in a recent study of various grades of commercial and retail acetone included 2-pentanone, 4-hydroxy-4-methyl- (diacetone alcohol) and toluene (Wahl et al. 2010).

Exposure to acetone may occur via inhalation or ingestion or by the dermal/ocular route. The main industrial health hazards are associated with inhalation of acetone vapor at high concentrations or via repeated skin and eye contact. Accidental overexposure to acetone is rare. Dermal absorption can occur, but is typically minimal compared with exposure via inhalation and oral routes (NTP 1991).

Every organ and tissue in the human body contains some acetone. Acetone is produced in the body as a result of the breakdown and utilization of stored fats and lipids for energy. Conditions such as strenuous physical exercise or prolonged dieting, which lead to a breakdown of fat in the body, may increase levels of acetone in the bloodstream. Acetone is continuously being excreted in the breath and urine of humans as a result of its high volatility and solubility in water (UNEP 1999).

Two pathways for the conversion of acetone to glucose have been proposed, 1) the methylglyoxal and 2) the propanediol pathways. The methylglyoxal pathway converts acetol, acetol to methylglyoxal, and subsequently methylglyoxal to glucose. The propanediol pathway converts acetol to L-1,2-propanediol by an unknown process. L-1,2-propanediol is converted to L-lactaldehyde by alcohol dehydrogenase, and L-lactaldehyde is converted to L-lactic acid by aldehyde dehydrogenase. Expression of these metabolic pathways in rat depends on induction of acetone oxygenase and acetol monooxygenase by acetone (HSDB 2012).

[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.
[4] The CPA "Red List" refers to chemicals 1) flagged as Benchmark 1 using the GreenScreen™ List Translator or 2) flagged as Benchmark 1 or 2 using the GreenScreen™ List Translator and further assessed and assigned as Benchmark 1. The most recent version of the GreenScreen™ List Translator should be used.
[5] The way you conduct assessments for transformation products depends on the Benchmark Score of the parent chemical (See Guidance).

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References:

HSDB 2012, Hazardous Substances Data Bank (HSDB), available at: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB, accessed February 2012.

NTP 1991, National Toxicology Program (NTP), "Toxicity Studies of Acetone in F344/N Rats and B6c3f1 Mice (Drinking Water Studies)," available at: http://ntp.niehs.nih.gov/ntp/htdocs/ST_rpts/tox003.pdf, accessed February 2012.

UNEP 1999, United Nations Environment Program (UNEP), SIDS Initial Assessment Report http://www.chem.unep.ch/irptc/sids/OECDSIDS/67641.pdf, accessed February 2012.

Wahl et al. 2010, Jon H. Wahl, Cinnamon D. Bolz, Karen L. Wahl, "Investigating Solvent Purity Using Comprehensive Gas Chromatography: A Study of Acetones," LCGC Europe, Volume 23, Issue 4, available at http://www.chromatographyonline.com/lcgc/article/articleDetail.jsp?id=666757&sk=&date=&pageID=2, accessed February 2012.

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Hazard Classification Summary Section:
Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M or L): L
Acetone was assigned a score of L based on information found. However, authoritative bodies such as IRIS have indicated there is insufficient data for classification of carcinogenicity. The decision to assign this endpoint a value of 'L' is based upon professional judgment of an Ecology Toxicologist and should be revisited regularly to see if additional data changes the initial score of L.

- The OECD conclusions as stated in the Screening Information Data Sheet (SIDS) Initial Assessment Profile: '*Teratogenic effects were not observed in rats and mice tested at 26,110 and 15,665 mg/m3, respectively. Lifetime dermal carcinogenicity studies in mice treated with up to 0.2 mL of acetone did not reveal any increase in organ tumor incidence relative to untreated control animals*.', available at: http://webnet.oecd.org/Hpv/UI/handler.axd?id=bd1c15e7-792e-41fe-90ae-6894165069be, accessed 4/2013.
- EPA's Hazardous Substances Database (HSDB) states: 'Acetone has been used extensively as a solvent vehicle in skin carcinogenicity studies and is not considered carcinogenic when applied to the skin. Acetone is relatively less toxic than many other industrial solvents…', available at: http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@na+ACETONE, accessed 4/2013.
- US EPA 1999 assessment reports that based on the Draft Revised Guidelines for Carcinogen Risk Assessment "data are inadequate for an assessment of the human carcinogenic potential of acetone. This weight-of-evidence determination is based on the availability of one human study of limited utility, no chronic animal studies, and no additional information on structural analogues with known carcinogenic potential." US EPA 1999, Toxicological Review of Acetone, available at: http://www.epa.gov/iris/toxreviews/0128tr.pdf, accessed May 2012.
- Listed as ACGIH A4 Not classifiable as a human carcinogen (insufficient data), Hazardous Substances Data Bank, available at: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB, accessed February 2012.
- Not listed as a known carcinogen by IARC, NTP, NIOSH, ISSCAN or CA Prop 65.

Mutagenicity/Genotoxicity (M) Score (H, M or L): L
Acetone was assigned a score of Low for mutagenicity based on negative studies for chromosomal aberration and gene mutation.

- A US EPA study reports that (US EPA 1999, Toxicological Review of Acetone, available at: http://www.epa.gov/iris/toxreviews/0128tr.pdf, accessed February 2012):
  - "[T]he genotoxicity of acetone has been well studied in *in vitro* assays, with the results almost entirely negative (ATSDR, 1994; OECD, 1998; U.S. EPA, 1988b; WHO, 1998). All studies cited in the GENE-TOX data base were negative, with the exception of one study for which no conclusion was drawn. Neither sister chromatid exchange (SCE) nor chromosome aberrations were induced in Chinese hamster ovary cells by acetone at a concentration not exceeding 1% in the culture flask with or without metabolic activation (Loveday et al., 1990). Acetone was also negative for inducing sister chromatid exchanges in human (Tucker et al., 1993) and nonhuman (Latt et al., 1981) cell types in the absence of metabolic activation. Acetone did not induce chromosome aberrations in vitro (Preston et al., 1981)." [References internal to the assessment.]
- REACH registration dossiers report on several reliability 1 and 2 studies that were negative for genotoxicity, including Salmonella mutagenicity, mammalian chromosome aberration, and a mammalian cell gene mutation assay. See the dossier for details: European Chemicals Agency, registration dossier for acetone, available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d998764-70a1-6fbe-e044-00144f67d249/DISS-9d998764-70a1-6fbe-e044-00144f67d249_DISS-9d998764-70a1-6fbe-e044-00144f67d249.html, accessed February 2012.

Reproductive Toxicity (R) Score (H, M, or L): *L*
Acetone was assigned a score of Low for reproductive toxicity based on weight of evidence.

- PPRC: The data base is limited by the absence of a two-generation reproduction study for acetone and the absence of reproduction studies via inhalation exposures. A two-generation study is available for isopropanol

(which metabolises to acetone). While modest reproductive effects have been reported for both the acetone and isopropanol studies, the doses required for adverse effects have been high.

- US EPA 1999 study reports US EPA Toxicological Review of Acetone, available at: http://www.epa.gov/iris/toxreviews/0128tr.pdf, accessed February 2012:
  - Several studies are evaluated for reproductive endpoints:
    - Larsen et al. (1991): Ten male rats (Mol/Wis., SPF) administered 0.5% acetone (5,000 ppm) in drinking water for six weeks and then bred to untreated females of the same strain; additional group of 10 males treated for six weeks followed by a 10-week recovery period prior to breeding.
    - NTP (1991) also published as Dietz et al. (1991): Groups of five male and five female F344/N rats were administered acetone in drinking water at concentrations ranging from 0, to 100,000 ppm for 14 days (~ 0 to 6,900 mg/kg-day for males and 0 to 8,600 mg/kg-day for females. Also, groups of 10 male and 10 female F344/N rats were administered acetone in the drinking water at concentrations ranging from 0 to 50,000 ppm for 13 weeks. (0 to 3,400 mg/kg-day for males and 0 to 3,100 mg/kg-day for females).
    - **Isopropanol** oral exposure: Bevan et al. (1995) two-generation reproduction toxicity study on rats with isopropanol. Thirty male and thirty female Sprague-Dawley rats (P1 generation) dosed by oral gavage with 0, 100, 500, and 1,000 mg/kg-day for at least 10 weeks prior to mating. The females dosed during mating, gestation and lactation while males dosed during mating and delivery. The second generation parental (P2) were selected from the offspring of the first generation (F1) and were dosed for 10-13 weeks before mating to produce a single litter.
  - Evaluation of acetone studies - pp. 32-33: "The NTP (1991) study authors state that the decrease in sperm motility at the highest dose was consistent with mild reproductive effects. These effects are characterized as consistent with mild toxic effects on spermatogenesis. The authors also noted that there were no morphological or histological effects seen microscopically. Data on the toxicity of acetone on male reproductive organs suggest that at high doses there is a mild testicular effect, as indicated by diminished sperm motility and malformed sperm. Larsen et al. (1991) indicate that at drinking water doses of 5,000 ppm there is no effect on male reproductive capacity. At comparable doses in the NTP (1991) and Dietz et al., (1991) studies, there were no detectable reproductive effects. It is unknown if the reduced sperm motility and higher percentage with malformations noted at 50,000 ppm [39,500 mg/L] translates into impaired reproductive ability."
  - Evaluation of Bevan - p. 48: "While there are no two-generation reproductive toxicity studies for acetone, data from isopropanol, which is metabolized primarily to acetone, may provide useful information. A two-generational gavage study (Bevan et al., 1995) in rats indicates that the only reproductive effect was a statistically significant reduction in the P2,but not P1, male mating index in the high dose group (1,000 mg/kg-day) which the study authors characterized as slightly below historical controls."
  - p. 62: "A reference concentration (RfC) has not been determined. There are no studies demonstrating conclusive effects either in humans or animals arising from chronic exposure. Confidence in the overall data base is low because little supporting data and no chronic or reproductive inhalation studies are available. Lack of sufficient evaluation of reproductive toxicity by either oral or inhalation exposure is considered a data base deficiency. Changes in testicular weight were observed in male rats following oral exposure and a premature menstrual period occurred in 3 of 4 women acutely exposed by inhalation. The significance of these endpoints of reproductive toxicity in men and women is unknown at this time."
  - References indicated are internal to the assessment.
- NITE/Japan 2006 ranks as Category 2, but this is based primarily on developmental effects. "There is a report that he has no effect on a miscarriage in an epidemiological study (ATSDR, 1994). It is reported of slight developmental toxicity (decrease of embryo weight) in rat high concentration exposure (11000 ppm (20 mg/L)) (EHC, 207 (1998)) and of the decrease of embryo weight and the increase of late embryo absortion rate in mouse high concentration exposure (6600 ppm (15.6 mg/L)) (EHC, 207 (1998)). There is a description that study is still more nearly required, for an animal with humans (EHC). And it is classified into the Category 2…" [References are internal to the assessment.] National Institute of Technology and Evaluation (Japan), information available at http://www.safe.nite.go.jp/english/ghs_index.html (substance ID 635), accessed February 2012.

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- UNEP 1999 reports: "Acetone showed minimal reproductive and developmental effects in animals exposed either by inhalation or via drinking water. No reproductive performance changes or testicular histopathological effects were noted in male rats treated with 0.5% acetone in their drinking water for 6 weeks (Larsen et al., 1991). In another study, however, an acetone drinking water concentration of 5% caused a mild decrease in testicular weight, a moderate increase in the incidence of abnormal sperm, and depressed sperm motility after 13 weeks of treatment (Dietz et al., 1991). These findings indicate that high concentrations of acetone can have a mild effect on rat spermatogenesis." [References are internal to the assessment.] UNEP SIDS Initial Assessment Report, available at: http://www.chem.unep.ch/irptc/sids/OECDSIDS/67641.pdf , p. 26, accessed February 2012.
- For the Dietz study reported above, the REACH registration dossiers notes that: "There was no indication of reproductive toxicity in male mice (NOEL 4,858 mg/kg bw/d) or female mice (NOEL 11,298 mg/kg bw/d)." See the dossier for details: European Chemicals Agency, registration dossier for acetone, available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d998764-70a1-6fbe-e044-00144f67d249/DISS-9d998764-70a1-6fbe-e044-00144f67d249_DISS-9d998764-70a1-6fbe-e044-00144f67d249.html, accessed February 2012.
- Full details of the Dietz et al. 1991 studies are available in the National Toxicology Program report "Toxicity Studies of Acetone (CAS No. 67-64-1) in F344/N Rats and B6c3f1 Mice (Drinking Water Studies)" accessible at: http://ntp.niehs.nih.gov/ntp/htdocs/ST_rpts/tox003.pdf.
- GHS guidance states that adverse effects seen in animal studies at very high dose are not normally sufficient for classification and suggests 1000 mg/kg as a possible limit dose (United Nations 2011, Globally Harmonized System of Classification and Labelling of Chemicals (GHS), Fourth revised edition, Section 3.7.2.5.9).
- US EPA Design for the Environment criteria suggest NOAEL/LOAEL > 1000 mg/kg/day would rank as very low hazard for reproductive and developmental toxicity. US EPA 2011, Design for the Environment (DfE) Program Alternatives Assessment Criteria for Hazard Evaluation, available at: http://www.epa.gov/dfe/alternatives_assessment_criteria_for_hazard_eval.pdf, accessed February 2012.

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

Acetone is assigned a score of Low for developmental toxicity based on weight-of-evidence. NITE/Japan (GreenScreen Screening A list) classifies acetone as Category 2 for developmental effects, but the effects observed in studies for both acetone and isopropanol occurred at high doses. While GreenScreen criteria do not include dose ranges for this endpoint, the criteria refer to GHS guidance which allows that adverse effects seen in animal studies at very high dose are not normally sufficient for classification (United Nations 2011, Globally Harmonized System of Classification and Labelling of Chemicals (GHS), Fourth revised edition, Section 3.7.2.5.8).

- US EPA 1999 Toxicological Review of Acetone, available at: http://www.epa.gov/iris/toxreviews/0128tr.pdf , accessed February 2012 [References are internal to the IRIS assessment.]:
  - The US EPA assessment reports (pp. 48-49, 59): "Inhalation studies by Mast et al. (1988) reported an increased incidence in skeletal malformations in rats and delayed skeletal development in mice at high exposures, although the types of malformations are inconsistent. The most consistent finding with exposure to acetone was decreased fetal weight at high exposure (86-92% of control at 6,600 ppm for mice, and 84-86% of control at 11,000 ppm for rats)…The significance of the fetal body weight effect is questioned in light of the minimal severity of the effect, and the negative findings of other parameters including resorptions, number of live births, and number of births per litter, which were comparable to controls."
  - **Isopropanol** studies: "The developmental effects of isopropanol have been studied by the oral route of exposure. Bevan et al. (1995) showed there was a decrease in the survival of F1 offspring at high doses of isopropanol (1,000 mg/kg-day), a decrease in body weight in high dose F1 male rats and F2 male and female rats, and no treatment-related abnormalities. Tyl et al. (1994) showed maternal toxicity at 800 and 1,200 mg/kg-day in rats and no evidence of developmental effects in offspring. The authors also reported decreases in fetal body weight at 480 mg/kg-day in rabbits with no other developmental effects noted. Gavage studies (Tyl et al., 1994) reported NOAELs of 400 and 480 mg/kg-day for rats and rabbits, respectively, based on reduced fetal weight. No effects were observed at doses up to 1,200 mg/kg-day on

postimplantation loss, litter size, sex ratio, or external, visceral, or skeletal abnormalities for either model." p. 49.
  - Referring to the oral route of exposure with **isopropanol**: "…Bates et al. (1994) found no evidence of neurobehavioral or morphological abnormalities from the prenatal administration of isopropanol by gavage to pregnant rats." p. 49.
- UNEP 1999 reports that: "The no-observed-effect level for developmental toxicity was found to be 5220 mg/m^3 for both rats and mice. Acetone did not produce any teratogenic effects at any of the exposure concentrations tested. The no-observed-effect level for teratogenicity was, therefore, greater than or equal to 15,665 mg/m^3 for mice and 26,110 mg/m^3 for rats." UNEP SIDS Initial Assessment Report available at: http://www.chem.unep.ch/irptc/sids/OECDSIDS/67641.pdf , p. 26, accessed February 2012.
- NITE/Japan, Category 2. Assessment states: "It is reported of slight developmental toxicity (decrease of embryo weight) in rat high concentration exposure (11000 ppm (20 mg/L)) (EHC, 207 (1998)) and of the decrease of embryo weight and the increase of late embryo absor[p]tion rate in mouse high concentration exposure (6600 ppm (15.6 mg/L)) (EHC, 207 (1998))…And it is classified into the Category 2…" [References are internal to the assessment.] National Institute of Technology and Evaluation (Japan), information available at: http://www.safe.nite.go.jp/english/ghs_index.html, (substance ID 635), accessed February 2012
- NITE/Japan 2006 results based on NTP studies TER87036 and TER87140. Also reported as the Mast et al. 1988 studies in the US EPA assessment. These studies considered the potential for acetone to cause developmental toxicity in Sprague-Dawley rats exposed to 0, 440, 2200, or 11000 ppm, and in Swiss (CD-1) mice exposed to 0, 440, 2200, and 6600 ppm acetone vapors, 6 h/day, 7 days/week. Each of the four treatment groups consisted of 10 virgin females (for comparison), and ~32 positively mated rats or mice. Positively mated mice were exposed on days 6-17 of gestation (dg), and rats on 6-19 dg. The day of plug or sperm detection was designated as 0 dg. Developmental toxicity was observed in mice in the 6600 ppm exposure group as: 1) a statistically significant reduction in fetal weight, and 2) a slight, but statistically significant increase in the percent incidence of late resorptions. However, the increase in the incidence of late resorptions was not sufficient to cause a decrease in the mean number of live fetuses per litter. The incidence of fetal malformations or variations in mice was not altered by exposure to acetone vapors at any of the levels employed…It may be concluded from the results of this study that the 2200-ppm acetone level was the no observable effect level (NOEL) in both the Sprague-Dawley (CD) rat and the Swiss (CD-1) mouse for developmental toxicity. Furthermore, since only minimal maternal toxicity was observed at 11000 ppm acetone for rats and 6600 ppm acetone for mice, it is possible that the actual maternal NOEL is somewhat greater than 2200 ppm." From abstract "Inhalation Developmental Toxicity Studies: Acetone (CAS # 67-64-1) in Mice and Rats," available at: http://ntp.niehs.nih.gov/index.cfm?objectid=07303007-0BC7-995C-A9EE87A225ABDEEE, accessed February 2012.
- PPRC: Mast et al. 1988 NOEL of 2200 ppm converts to 5.2 mg/L consistent with US EPA DfE low level-of-concern for reproductive and developmental toxicity. US EPA 2011, Design for the Environment (DfE) Program Alternatives Assessment Criteria for Hazard Evaluation, available at: http://www.epa.gov/dfe/alternatives_assessment_criteria_for_hazard_eval.pdf, accessed February 2012. Also, GHS guidance states that adverse effects seen in animal studies at very high dose are not normally sufficient for classification and suggests 1000 mg/kg as a possible oral limit dose (United Nations 2011, Globally Harmonized System of Classification and Labelling of Chemicals (GHS), Fourth revised edition, Section 3.7.2.5.8 and 3.7.2.5.9).

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

Acetone was assigned a score of DG for endocrine activity based on lack of data.

- Acetone was not listed as an endocrine disruptor in the following lists:
  - European Union Priority List of suspected endocrine disruptors.
  - OSPAR Convention for The Protection of the Marine Environment of the North-East Atlantic, List of Chemicals for Priority Action and List of Substances of Possible Concern
  - International Chemical Secretariat (ChemSec) Substitute it Now (SIN) List 2.0
  - The Endocrine Disruptor Exchange (TEDX) List of Potential Endocrine Disruptors
- No specific test data excluding endocrine activity was identified.

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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

Acetone was assigned a score of Low for acute mammalian toxicity based on lethal dose/concentration data in animal studies consistent with a low level-of-concern by all exposure pathways.

- Hazardous Substances Data Bank, available at: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB, accessed February 2012:
  - Oral exposure: variety of mouse, rat and rabbit LD_{50}'s > 3000 mg/kg
  - Dermal exposure: rabbit LD_{50} at 20,000 mg/kg
  - Inhalation exposure: rat LC_{50}s reported as 76 mg/L/4 hr and 50.1 mg/L/8 hr
- NITE/Japan 2006, spreadsheet identifier: ID 635, available at: http://www.safe.nite.go.jp/english/ghs_index.html, accessed February 2012:
  - Oral exposure: Rat LD_{50} > 5000 mg/kg
  - Dermal exposure: Rat LD_{50} > 5000 mg/kg
  - Inhalation exposure: vapor - Rat LC_{50} = 32,000 ppm (75.8 mg/L)
  - Aspiration - Category 2; included for reference. Not used for ranking as this endpoint is not included in the classification system.

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)
Group II Score (single dose: vH, H, M or L): L

Acetone was assigned a score of Low for systemic toxicity/organ effects based on overall low toxicity and the mild and transient effects reported for repeat-dose toxicity.

- NITE/Japan 2006 reports Category 3 for respiratory tract irritation and narcosis (narcosis relevant only to neurotoxicity endpoint); based on 2001 ACGIH data. Country GHS assessments are GreenScreen Screening A lists and Category 3 translates to Moderate level-of-concern. While the NITE/Japan 2006 GHS category 3 translates to Moderate level-of-concern (for respiratory irritancy and narcosis), the more recent UNEP SIDS assessment (below) discounts irritancy. Furthermore, a ranking based on narcosis applies to the GreenScreen neurotoxicity endpoint. NITE/Japan, spreadsheet identifier: ID 635, available at: http://www.safe.nite.go.jp/english/ghs_index.html, accessed February 2012.
- UNEP 1999 assessment reports: "The inhalation EHE [estimated short-term human exposure] values for occupational and consumer groups have been set at 1780 and 900 mg/m^3, respectively. The most critical effect of acetone inhalation for both industrial and consumer contact is central nervous system depression. This endpoint was selected over the more commonly reported sensory irritation effects based on the findings from a recently completed comprehensive review of the odor and irritancy potential of acetone (Arts et al., 1998). The authors of this review concluded that subjective reports of acetone's irritancy were unreliable and likely related to its distinctive odor. Furthermore, the authors determined that the true irritancy threshold for acetone vapors was very high, ranging somewhere between 23,730 and 94,930 mg/m^3." [References are internal to the assessment.] UNEP SIDS Initial Assessment Report available at: http://www.chem.unep.ch/irptc/sids/OECDSIDS/67641.pdf, p. 29, accessed February 2012.

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

Acetone was assigned a score of Low based on weight-of-evidence. Effects noted in both humans and animals occurred at doses greater than 1.0 mg/L/6h/day (inhalation exposure) and 100 mg/kg-bw/day (oral exposure) which are above the range for GHS categorization.

- NITE/Japan 2006 assessment reports Category 2 for damage to organs (blood) through prolonged or repeated exposure. "It was classified into Category 2, since by the examination using volunteers, the significant increase

in white corpuscles and an eosinophil and the significant reduction of a phagocytosis of a neutrophil were observed in the exposure group with 500 ppm [1.2 mg/L], 6 hours/day for 6 days (ACGIH (2001)).” NITE/Japan 2006 assessment, spreadsheet identifier: ID 635, available at: http://www.safe.nite.go.jp/english/ghs_index.html, accessed February 2012. The ACGIH data was not identified.

- The NITE 2006 assessment likely refers to data reported in the 1994 review by the ATSDR (Agency for Toxic Substances and Disease Registry 1994, Toxicological Profile for Acetone, available at: http://www.atsdr.cdc.gov/toxprofiles/tp21.pdf, accessed February 2012. [References internal to the assessment.]):
  - p. 29: “The only information regarding immunological effects in humans after inhalation exposure to acetone is the finding of statistically significant increased white blood cell counts, increased eosinophil counts, and decreased phagocytic activity of neutrophils in volunteers exposed to 500 ppm [1.2 mg/L] for a single 6-hour exposure or intermittently for 6 days (Matsushita et al. 1969a, 1969b). No significant difference in these parameters was seen in the volunteers exposed to 250 ppm compared with controls. Hematological parameters, including total white cell counts and differential white cell counts, were within normal limits in other volunteers exposed to 500 ppm for 2 hours (DiVincenzo et al. 1973) or <1,250 ppm acetone intermittently for durations in a study with a complex protocol (Stewart et al. 1975); however, these investigators did not examine the phagocytic activity of neutrophils. The NOAEL value of 250 ppm and LOAEL value of 500 ppm …”
  - pp. 155-6: “Information regarding immunological effects in humans after exposure to acetone is limited. Significantly increased white blood cell counts, increased eosinophil counts, and decreased phagocytic activity of neutrophils were found in volunteers exposed by inhalation (Matsushita et al. 1969a, 1969b), but a battery of immune function tests has not been performed.”
  - Woolhiser et al. (2006): “This study was designed to investigate the immunotoxicity potential of acetone in mice following a more direct systemic route of dosing via drinking water for 28 days. CD-1 male mice consumed average daily acetone doses of 121, 621 or 1144 mg/kg/day…[T]he direct systemic administration of acetone did not produce evidence for immunotoxicity in CD-1 mice and the no observed adverse effect level (NOAEL) in this study was determined to be 1144 mg/kg/day.” Additional details available in Woolhiser et al., “Acetone in drinking water does not modulate humoral immunity in mice as measured by the antibody, plaque-forming cell assay,” Int. J. Toxicol. 2006 Sep-Oct; 25(5):333-9. Abstract at: http://www.ncbi.nlm.nih.gov/pubmed/16940005?dopt=Abstract, accessed February 2012.
- US EPA 1999 assessment reports (US EPA Toxicological Review of Acetone, available at: http://www.epa.gov/iris/toxreviews/0128tr.pdf, p. 61, accessed February 2012) [References are internal to the assessment]:
  - “No human studies following oral exposure to acetone are available. Studies on rodent exposure to orally-administered acetone have identified several treatment-related health effects. Subchronic oral exposure resulted in kidney, testis, and hematologic system effects; however, the effects were characterized as mild. Although the nephrotoxic effects noted in rodents have been identified as the most critical effects, they tend to occur in male rats only and at high levels of exposure (20,000 and 50,000 ppm in drinking water).
  - 20,000 and 50,000 ppm concentrations correspond to 1700 and 3400 mg/kg/day (UNEP SIDS, see reference below).
  - “Inhalation studies in humans have been conducted on both volunteers and occupationally-exposed individuals (Dick et al., 1988, 1989; Kiesswetter et al., 1994; Stewart et al., 1975). These studies have examined, almost exclusively, either the toxicokinetics or neurological effects of acetone. The effects reported in these studies appear to be mild and transient.”
- UNEP 1999 assessment reports (referring to the NTP 1001 study): “In a subchronic drinking water study, renal toxicity and increased liver and decreased spleen weights were observed. The reported NOAEL’s were 900mg/kg/d and 3,100 mg/kg/d for male and female rats, and 2,258 mg/kg/d and 5,945 mg/kg/d for male and female mice.” UNEP SIDS Initial Assessment Report available at: http://www.chem.unep.ch/irptc/sids/OECDSIDS/67641.pdf, p. 29, accessed February 2012.

- Oral exposure: The data cited in the NITE, US EPA, and UNEP studies above refer to an NTP study by Dietz using F344/N rats and BGCSFi mice (ten males and ten females of each species). The study concludes that acetone is mildly toxic to rats and mice when administered in drinking water for 13 weeks. "Minimal toxic doses were estimated to be 20,000 ppm acetone for male rats and male mice and 50,000 ppm acetone for female mice. No toxic effects were identified for female rats. Acetone doses used during the 13-week studies were equivalent to 200-3,400 mg/kg per day for rats and 380-11,298 mg/kg per day for mice. The species/sex most sensitive to acetone toxicity, based on the minimal toxic dose, is the male rat (1,700 mg/kg per day), followed by the male mouse (4,858 mg/kg per day), female mouse (11,298 mg/kg per day), and female rat (minimal toxic dose not identified). The testis, kidney, and hematopoietic system were identified as target organs for male rats, and the liver was the target organ for male and female mice. NTP study report "Toxicity Studies of Acetone in F344/N Rats and B6c3f1 Mice (Drinking Water Studies)," available at: http://ntp.niehs.nih.gov/ntp/htdocs/ST_rpts/tox003.pdf, accessed February 2012.
- Data from European Chemicals Agency, REACH registration dossier for acetone, available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d998764-70a1-6fbe-e044-00144f67d249/DISS-9d998764-70a1-6fbe-e044-00144f67d249_DISS-9d998764-70a1-6fbe-e044-00144f67d249.html, accessed February 2012:
  - Inhalation exposure study by Bruckner (1991): Sprague-Dawley rats were exposed to acetone by inhalation, 5 days/wk, 3 hrs/day at a single dose corresponding to 45,000 mg/m^3 for 2, 4 or 8 weeks. The dossier concludes: "Under the conditions of this exposure there were no indications of an adverse toxic effect from the investigated endpoints being body weight gain, organ weights (liver, kidney, brain, lung; N=5), histopathology of liver, kidney, brain, lung, and heart (N=4) and serum clinical chemistry parameters (SGOT, LDH and BUN; N=5). Slight significant decreases of weights of brain (at 4 and 8 w of exposure) and of kidney (only at 4 w of exposure) correlated with a depression of body weight gain (not significant) and were without a histological correlate. Based on the investigated endpoints the NOAEC is 19,000 ppm acetone or 45,000 mg/m^3."
  - Dermal exposure: The dossier includes a weight-of-evidence summary of acetone exposure when used as a vehicle for other chemical agents. The dossier concludes: "Acetone has been applied as solvent in several dermal carcinogenicity studies with different strains of mice. Consequently, there is experience with up to lifetime dermal exposure to low doses of acetone with test volumes of 0.025 to 0.2 ml corresponding to doses of ca. 20 to 160 mg acetone/mouse with 2 or 3 treatments per week for up to lifetime (up to 573 days). In these studies no noticeable effects on survival or incidence of skin neoplasms was described for the acetone-treated solvent control groups. No other endpoints were examined. Principally, these data point in the direction that the low acute dermal toxicity of acetone would be confirmed upon chronic administration. Additionally, due to the volatility of acetone, standard conditions of dermal application will result in considerable evaporation from the skin surface so that the effective dose for dermal uptake will be reduced. Consequently, a dermal repeated dose toxicity study does not seem to be scientifically justified.

Neurotoxicity (N)
Group II Score (single dose: vH, H, M or L): M
Acetone was assigned a score of Moderate for neurotoxicity based on GHS classification consistent with Category 3. GHS category 3 translates to a Moderate level-of-concern.

- Grandjean & Landrigan 2006 list acetone as a human neurotoxicant. This Screening B list translates to GreenScreen vH, H or M. Grandjean & Landrigan 2006, Developmental neurotoxicity of industrial chemicals, Lancet, v. 368: 2167–78.
- The US EPA 1999 assessment reports: "Inhalation exposures led to ataxia and central nervous system depression in animal studies; effects were transient with full recovery." pp. 38-39. "The neurotoxic effects noted in humans are reported to be both mild and transient." p. 47. US EPA Toxicological Review of Acetone, available at: http://www.epa.gov/iris/toxreviews/0128tr.pdf, accessed February 2012.
- The transient narcotic effects reported in the US EPA 1999 assessment are consistent with GHS specific target organ toxicity, single-exposure Category 3. United Nations 2011, Globally Harmonized System of Classification and Labelling of Chemicals (GHS), fourth revised edition, Section 3.8.2.2.

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- European Union harmonized classification reported as H336, R67: Vapours may cause drowsiness and dizziness. This Authoritative B list translates to M or L. Classifications available at: http://clp-inventory.echa.europa.eu/SummaryOfClassAndLabelling.aspx?SubstanceID=22981&HarmOnly=no?fc=true&lang=en, accessed February 2012.
- UNEP 1999 assessment reports that: "Mild neurobehavioral changes have been observed in rats repeatedly exposed to high vapor concentrations of acetone...Acetone concentrations of 28,480 and 37,975 mg/m^3 produced ataxia in several animals after a single exposure, however, a rapid tolerance developed and ataxia was not seen on subsequent days." p. 26-27. Summary reports that: "Acetone is therefore considered to have a low potential for neurological risk to humans." p. 28. UNEP SIDS Initial Assessment Report available at: http://www.chem.unep.ch/irptc/sids/OECDSIDS/67641.pdf, accessed February 2012.

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

Because of the conflicting information, the PPRC assessor requested an expert review of the data. Dr. Alex Stone reviewed the following information and assigned acetone a rank of Moderate for repeat dose neurotoxicity. This decision was based upon the European Union harmonized classification as H336, R67 and the identification of the chemical by Grandjean & Landrigan as a potential neurotoxicant. These identifications are also supported by select studies in the sources reported below. The classification of Moderate was also selected as it conservatively identified the level-of-concern. New studies will likely clarify the seriousness of this endpoint and should be reviewed as available for future updates.

- The US EPA 1999 assessment reports (US EPA Toxicological Review of Acetone, available at: http://www.epa.gov/iris/toxreviews/0128tr.pdf, p. 47, accessed February 2012) [References noted are internal to the assessment.]:
  - "Data on the neurotoxic effects of acetone are limited to inhalation exposure. The neurotoxic effects noted in humans are reported to be both mild and transient. Mitran et al. (1997) reported statistically significant reductions in nerve conduction velocity in workers. Animal data are generally consistent with the effects noted in humans. Other studies demonstrate transient impaired learning or response following inhalation exposure in rodents (CMA, 1997). This is consistent with the relatively nonpolar, lipophilic properties of acetone, which enhances its ability to cross the blood-brain barrier. As acetone is lost from the system, either by excretion or metabolism, irritation and other neurotoxic effects subside." p. 47.
  - Isopropanol inhalation (isopropanol is metabolized mainly to acetone): "Burleigh-Flayer et al. (1994) conducted an inhalation neurotoxicity study on CD-1 mice and Fischer rats. Five groups of rats or mice (10/sex) were exposed to isopropanol at concentrations of 0, 100, 500, 1,500 and 5,000 ppm for 6 hours/day, 5 days/week for 13 weeks. The study authors report that during exposure, some animals demonstrated narcosis, ataxia, and hypoactivity. This effect was not seen in rats following the first week of the study. Female rats demonstrated a 57% increase in motor activity in the 5,000 ppm group at weeks nine and 13. Otherwise, there were no changes in any of the parameters of the functional observational battery. No effects were seen with males. The authors report an increase in body weight and body weight gain in female rats in the 5000 ppm group which corresponded with increased food and/or water consumption." p. 42.
  - Isopropanol inhalation: "In a subchronic study, Burleigh-Flayer et al. (1998) conducted neurotoxicity evaluations on CD-1 mice and Fisher F344 rats. The animals were exposed to concentrations of 0, 100, 500, 1,500, or 5,000 ppm of isopropanol for 6 hours/day and 5 days/week for 13 weeks. The study authors reported ataxia, narcosis, hypoactivity, and/or a lack of a startle response following exposure in some rats or mice in the 5,000 ppm group and in some mice in the 1,500 ppm group. In the functional observational battery, none of the males exhibited statistically significant effects compared with the control group while motor activity increased in the female group following either 9- or 13-week exposures in the 5,000 ppm group. In a follow-up study, two groups of 30 female Sprague-Dawley rats were exposed to concentrations of either 0 or 5,000 ppm of isopropanol. The two groups were divided into either 9- or 13-week sessions, and spontaneous motor activity was assessed after 4, 7, 9, 11, and 13 weeks of exposure. A statistically significant increase in motor activity was observed after 4 weeks of exposure compared with the control group. The increased activity was not evident 2 days after cessation of the 9-week exposure or 2 weeks after cessation of the 13-week exposure." p. 43.

- UNEP 1999 assessment reports: "Mild neurobehavioral changes have been observed in rats repeatedly exposed to high vapor concentrations of acetone. Female rats were exposed 4 hr/day for 2 weeks at acetone concentrations of 7120, 14240, 28480, and 37975 mg/m^3 were examined for their response to avoidance and escape stimuli before and after each exposure (Goldberg et al., 1964). Repeated daily exposures to 14,240 mg/m^3 of acetone produced an inhibition of avoidance behavior but did not produce any signs of motor imbalance. Acetone concentrations of 28,480 and 37,975 mg/m^3 produced ataxia in several animals after a single exposure, however, a rapid tolerance developed and ataxia was not seen on subsequent days. In a recent schedule controlled operant performance study, acetone did not cause any permanent effects in rats exposed to the vapor for 13 weeks at 2375, 4750, and 9495 mg/m3 (Christoph and Stadler, 1997)." [References are internal to the assessment.] UNEP SIDS Initial Assessment Report available at: http://www.chem.unep.ch/irptc/sids/OECDSIDS/67641.pdf, pp. 26-27, accessed February 2012.
- European Union harmonized classification reported as H336, R67: Vapours may cause drowsiness and dizziness. This Authoritative B list translates to M or L. European Chemicals Agency Classification and Labelling Inventory Database available at: http://clp-inventory.echa.europa.eu/SummaryOfClassAndLabelling.aspx?SubstanceID=22981&HarmOnly=no?fc=true&lang=en, accessed May 2012.
- Grandjean & Landrigan 2006 list acetone as a human neurotoxicant. This Screening B list translates to GreenScreen vH, H or M. Grandjean & Landrigan 2006, Developmental neurotoxicity of industrial chemicals, Lancet, v. 368: 2167–78.

Skin Sensitization (SnS) Group II* Score (H, M or L): L
Acetone was assigned a Low level-of-concern for skin sensitization based on QSAR and experimental results suggesting no sensitization.

- NITE/Japan 2006 assessment reports: "Since it was indicated negative by the Mouse ear swelling test and Guinea pig maximization test (SIDS (1999)), the skin sensitization was put outside of the Category." Not classified. Screening A list translates to Low level-of-concern. NITE/Japan 2006 assessment, spreadsheet identifier: ID 635, available at: http://www.safe.nite.go.jp/english/ghs_index.html, accessed February 2012.
- UNEP 1999 assessment reports: "Acetone did not cause contact hypersensitization in the mouse ear swelling test or the guinea pig maximization test (Descotes, 1988; Nakamura et al., 1994)." [References are internal to the assessment.] UNEP SIDS Initial Assessment Report available at: http://www.chem.unep.ch/irptc/sids/OECDSIDS/67641.pdf, Summary on p. 25 with additional experimental details reported in the data sheets p. 87, accessed February 2012.
- A REACH registration dossier reports both QSAR and experimental results (European Chemicals Agency, REACH registration dossier for acetone, available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d998764-70a1-6fbe-e044-00144f67d249/DISS-9d998764-70a1-6fbe-e044-00144f67d249_DISS-9d998764-70a1-6fbe-e044-00144f67d249.html, accessed February 2012):
  - CAESAR QSAR model for Skin Sensitization v.1.0.0.8, classified as Inactive.
  - 1994 reliability 2 study; no guideline reported and no data given on GLP compliance. Guinea Pig Maximization test: "No indications of a sensitizing potential of acetone were found in a guinea pig maximization test."
  - 1988 reliability 2 study; no guideline reported and no data given on GLP compliance. Mouse ear swelling test: "Absence of a sensitizing potential of acetone was demonstrated in the mouse ear swelling assay."

Respiratory Sensitization (SnR) Group II* Score (H, M or L): DG
Acetone was assigned a score of DG for respiratory sensitization based on lack of relevant data.

- NITE/Japan 2006 assessment reports: "Since there is no data, the respiratory sensitization cannot be classified." NITE/Japan, spreadsheet identifier: ID 635, available at: http://www.safe.nite.go.jp/english/ghs_index.html, accessed February 2012.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M or L): L
Acetone was assigned a score of Low for skin irritation/corrosivity based on NITE/Japan (GHS Not Classified) and UNEP SIDS assessments of data.

- NITE/Japan 2006 assessment reports: Not classified. "It was classified as out of Category from the statement of having no stimulativeness on rabbit skin (EHC 207 (1998)) and (SIDS (1999))." [References are internal to the assessment.] NITE/Japan, spreadsheet identifier: ID 635, available at: http://www.safe.nite.go.jp/english/ghs_index.html, accessed February 2012.
- UNEP 1999 assessment reports: "Acetone is not a skin irritant or sensitiser but is a defatting agent to the skin." UNEP SIDS Initial Assessment Report available at: http://www.chem.unep.ch/irptc/sids/OECDSIDS/67641.pdf, p. 3, accessed February 2012.
- REACH registration dossier includes a 1986, reliability 2 study, no guideline reported and no data on GLP status. Dunkin-Harley guinea pigs treated three times per day for three days with 10 ul, open coverage. Significant departures from current preferred OECD methods. Summary states: "Acetone showed no irritant action to the skin of guinea pigs based on any endpoint of this test model, whereas methylethyl ketone induced a slight irritant response, and trichlorethylene and white spirit produced the most marked responses." European Chemicals Agency 2012, REACH registration dossier for acetone, available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d998764-70a1-6fbe-e044-00144f67d249/DISS-9d998764-70a1-6fbe-e044-00144f67d249_DISS-9d998764-70a1-6fbe-e044-00144f67d249.html, accessed February 2012.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L): H
Acetone was assigned a score of High for eye irritation/corrosivity based on EU GHS classification as Category 2, H319 (GreenScreen Authoritative A List).

- European Union harmonized classification as Category 2, H319: Causes serious eye irritation. European Chemicals Agency Classification and Labelling Inventory Database available at: http://clp-inventory.echa.europa.eu/SummaryOfClassAndLabelling.aspx?SubstanceID=22981&HarmOnly=no?fc=true&lang=en, accessed May 2012.
- NITE/Japan 2006 assessment reports: "Vapor stimulates public eye. However, if exposure stops, irritation will not follow (ATSDR (1994)). The result of severe is reported in the rabbit (ACGIH (2001)). Although a corneal epithelium is destroyed, substrate is not destroyed, and destruction of a corneal epithelium will be recovered in 4-6 days. Acetone is not corrosive eye irritations (SIDS (1999)). It was set as Category 2B from the above description." 2B on a Screening A list translates to M level-of-concern. NITE/Japan, spreadsheet identifier: ID 635, available at: http://www.safe.nite.go.jp/english/ghs_index.html, accessed February 2012.

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M or L): L
Acetone was assigned a score of Low for acute aquatic toxicity based on test data for fish and aquatic invertebrates.

- REACH dossier reports a large number of studies for fish, invertebrates and algae. These values are consistent with Low aquatic toxicity. European Chemicals Agency 2012, REACH registration dossier for acetone, available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d998764-70a1-6fbe-e044-00144f67d249/DISS-9d998764-70a1-6fbe-e044-00144f67d249_DISS-9d998764-70a1-6fbe-e044-00144f67d249.html, accessed February 2012.
- NITE/Japan 2006 assessment reports Not Classified based on study reporting acute aquatic toxicity LC_{50} (96 hr) > 100 mg/L (fathead minnows). NITE/Japan, spreadsheet identifier: ID 635, available at: http://www.safe.nite.go.jp/english/ghs_index.html, accessed February 2012.
- HSDB reports results from a large number of peer reviewed studies, mostly for fish. Typical LC_{50} values > 5000 mg/L/96-hr. HSDB results available at http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB, accessed February 2012.
- UNEP 1999 SIDS Initial Assessment Report (available at: http://www.chem.unep.ch/irptc/sids/OECDSIDS/67641.pdf, accessed February 2012) summarizes toxicity data:
  - p. 6 - Acute Toxicity to Aquatic Invertebrates: LC_{50} (mg/L): Nitocra spinipes - 16,700; Daphnia magna - 15,800; Daphnia pulex - 8800; Daphnia cucullata - 7635; Artemia salina - 2100."

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- p. 6 - Acute/Prolonged Toxicity to Fish LC_{50} (mg/L): Fathead minnow - 15,000; Japanese medaka - 14,300; Mosquito fish - 13,000; Goldfish - >5000; Golden orfe - 9880; Bluegill sunfish - 8300; Rainbow trout - 7400; Brook trout - 6070.

Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): L
Acetone was assigned a score of Low for chronic aquatic toxicity based on test data for aquatic invertebrates and estimates for fish chronic toxicity.

- REACH registration dossier reports a1983 reliability 2 study, no data on GLP compliance; test comparable to OECD 211. 28-day-chronic toxicity of acetone to Daphnia magna studied under flow through conditions. Nominal concentrations of 0 (control), 545, 1106, 2212, 4344, 8689 mg/L. The 28-day NOEC based on reproduction was found to be 2212 mg/L (nominal). The 28-day NOEC (MATC) and 28 -day LOEC based on mortality of parent individuals was >1106 and < 2212 mg/L and 2212 mg/L (nominal), respectively. European Chemicals Agency 2012, REACH registration dossier for acetone, available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d998764-70a1-6fbe-e044-00144f67d249/DISS-9d998764-70a1-6fbe-e044-00144f67d249_DISS-9d998764-70a1-6fbe-e044-00144f67d249.html, accessed February 2012.
- UNEP 1999 assessment reports Chronic Toxicity to Aquatic Invertebrates NOEC (mg/L): Ceriodaphnia dubia - 1866, Daphnia magna - 1660. (Same study as REACH dossier above.) UNEP SIDS Initial Assessment Report available at: http://www.chem.unep.ch/irptc/sids/OECDSIDS/67641.pdf, p. 3, accessed February 2012.
- US EPA PBT Profiler estimates Fish ChV = 370 mg/L. US EPA PBT Profiler, found at http://www.pbtprofiler.net/default.asp, accessed February 2012. (Appendix A)

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): *vH*
Acetone was assigned a score of very High for persistence based on its half-life in air (> 5 days).

- US EPA's PBT Profiler estimates: Half-life in Air / Water / Soil / Sediment = 79 / 15 / 30 / 140 days. Media distribution, Air / Water / Soil / Sediment = 13% / 44%/ 43% / 0%. A total of 87% expected to distribute to water & soil. Significant distribution to air and half-life in air consistent with Very High level-of-concern. US EPA PBT Profiler, found at http://www.pbtprofiler.net/default.asp, accessed February 2012. (Appendix A)
- Environment Canada lists acetone as persistent. The screening-B list translates to a vH or H level-of-concern. Environment Canada Domestic Substances List, available at: http://www.ec.gc.ca/lcpe-cepa/eng/subs_list/DSL/DSLsearch.cfm, accessed February 2012.
- UNEP 1999 assessment reports: "Two processes govern the photochemical removal of acetone from the troposphere: reaction with hydroxyl radicals and photolysis. The two processes occur at about equal rates in clear unpolluted skies yielding a total tropospheric lifetime of about 32 days (Meyrahn et al., 1986). The reaction with hydroxyl radicals will predominate over photolysis in urban areas where hydroxyl radical concentrations are greater, and during cloudy winter-time conditions where photodecomposition is minimal. Rain out and other forms of wet deposition are considered to be minor tropospheric removal processes (Chatfield et al., 1987)." [References are internal to the assessment.] UNEP SIDS Initial Assessment Report available at: http://www.chem.unep.ch/irptc/sids/OECDSIDS/67641.pdf, p. 3, accessed February 2012.

Bioaccumulation (B) Score (vH, H, M, L, or vL): vL
Acetone was assigned a score of very Low for bioaccumulation based on measured values of log K_{ow} (log $K_{ow} \leq 4$).

- Calculation reported in REACH data submission: QSAR estimate using BCFBAF v.3.00: Log BCF =0.50; BCF =3.16 L/kg wet wt (regression-based estimate), Biotransformation half-life =0.0355 days (normalized to 10 g fish), Log BAF = -0.03, BAF =0.929 L/kg wet-wt (Arnot-Gobas upper trophic). BCF < 100 consistent with Very Low level-of-concern. REACH dossier available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d93c40d-8ae7-6966-e044-00144f67d249/AGGR-d08e810b-f3b7-492a-8d9d-c339f334fa79_DISS-9d93c40d-8ae7-6966-e044-00144f67d249.html#AGGR-d08e810b-f3b7-492a-8d9d-c339f334fa79, accessed February 2012.

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- HSDB cites log K_{ow} = -0.24 as an experimental value from measurements reported in Hansch, C., et al., "Exploring QSAR Hydrophobic, Electronic and Stearic Constants," Washington DC: Amer Chem Soc p. 6 (1995). HSDB results available at: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB , accessed February 2012.
- US EPA PBT Profiler estimates BCF at 3.2. US EPA PBT Profiler, found at http://www.pbtprofiler.net/default.asp, accessed February 2012. (Appendix A)

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M or L): L
Acetone was assigned a score of Low for reactivity based on hazard classifications and chemical structure inconsistent with explosive or reactive properties.

- HSDB reports NFPA 704 classification as 0 for reactivity. "Reactivity: 0.0= This degree includes materials that are normally stable, even under fire exposure conditions, and that do not react with water." HSDB results available at http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB, accessed February 2012.
- NITE/Japan 2006 assessment reports: "There are no chemical groups associated with explosive properties present in the molecules." NITE/Japan 2006 assessment, spreadsheet identifier: ID 635, available at: http://www.safe.nite.go.jp/english/ghs_index.html, accessed February 2012.
- US Department of Transportation (DOT) reports acetone as DOT Hazard Class 3 (flammable liquid), but otherwise not classified as explosive. DOT classifications available at: http://www.phmsa.dot.gov/portal/site/PHMSA/menuitem.ebdc7a8a7e39f2e55cf2031050248a0c/?vgnextoid=d84ddf479bd7d110VgnVCM1000009ed07898RCRD&vgnextchannel=4f347fd9b896b110VgnVCM1000009ed07898RCRD&vgnextfmt=print , accessed February 2012.

Flammability (F) Score (vH, H, M or L): H
Acetone was assigned a score of High for flammability based on EU hazard phrase H225 (GreenScreen Authoritative A list).

- European Union harmonized classification as Category 2, H225 "Highly flammable liquid and vapour." European Chemicals Agency Classification and Labeling Inventory Database available at: http://clp-inventory.echa.europa.eu/SummaryOfClassAndLabelling.aspx?SubstanceID=22981&HarmOnly=no?fc=true&lang=en, accessed May 2012.
- NITE/Japan 2006 assessment reports Category 2, Flash Point: -4 deg F. NITE/Japan 2006 assessment, spreadsheet identifier: ID 635, available at: http://www.safe.nite.go.jp/english/ghs_index.html, accessed February 2012.

References
References provided within individual endpoint results.

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Abbreviations / Acronyms / Initialisms

ACGIH	American Conference of Industrial Hygienists
ASTDR	Agency for Toxic Substances and Disease Registry
CAMEO	CAMEO Chemicals Database of Hazardous Materials
CEPA-DSL	Canadian EPA Domestic Substances List
ChemSec	International Chemical Secretariat [prepares the Substitute it Now (SIN) List]
CPA	Clean Production Action
ECCSP	Environment Canada Chemical Substances Portal
EC-EDD	European Commission endocrine disrupting substance database
ECHA C&L	ECHA Classification and Labeling Inventory Database
ECHA	European Chemicals Agency
EPA HPV	US EPA High Production Volume Information System
EPA SRS	US EPA Substance Registry System
ESIS	European chemical Substances Information System
EU	European Union
GHS	Globally Harmonized System (of classification and labeling)
HSDB	Hazardous Substances Data Bank
IARC	International Agency for Research on Cancer
IPCS	International Program on Chemical Safety
IRIS	Integrated Risk Information System (US EPA)
ISSCAN	Chemical carcinogens database (Italy)
J-Check	Japan Chemicals Cooperative Knowledge database
KEMI	Swedish Chemicals Agency
MSDS	Material Safety Data Sheet
NFPA	National Fire Protection Association
NIOSH	National Institute of Occupational Safety and Health
NITE	National Institute of Technology and Evaluation (Japan)
NTP	National Toxicology Program
OECD	Organization for Economic Co-operation and Development
OSPAR	Oslo Paris Commission and convention for protection of the marine environment
PBT Profiler	US EPA's PBT Profiler
Prop 65	California Proposition 65 regulation and list of chemicals of concern
REACH	European Commission chemicals regulation
RoC	Report on Carcinogens (National Toxicology Program)
RTECS	Registry of Toxic Effects of Chemical Substances
SIDS	Screening Information Data Sets
TEDX	The Endocrine Disruptor Exchange
UNEP	United Nations Environment Program
US DOT	US Department of Transportation Hazardous Materials Regulations
US EPA	United States Environmental Protection Agency

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Appendix A – US EPA PBT Profiler Results

Results

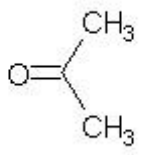
Orange or **red** highlights indicate that the EPA criteria have been exceeded.
Black-and-white version

Persistence	Bioaccumulation	Toxicity

67-64-1 2-Propanone

PBT Profiler Estimate = PBT

Media	Half-Life (days)	Percent in Each Medium	BCF	Fish ChV (mg/l)
Water	**15**	44%	**3.2**	**370**
Soil	**30**	43%		
Sediment	**140**	0%		
Air	**79**	13%		



P2 Considerations and more information .