



# TOXICOLOGY PROFILE

## ACETONE IN THE HEALTH CARE INDUSTRY

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## Summary

This report includes information related to acetone, including its chemical and physical properties, exposure routes, metabolism and pharmacokinetics, health effects, regulations, and control measures.

Acetone is a widely used solvent with high volatility, so it may be an airborne hazard in multiple occupational settings. Exposure routes include inhalation, dermal contact and accidental ingestion. Acetone presents naturally in our body from breaking-down of fat. Acetone is metabolized quickly once absorbed, with biological half-time of 2~4 hours.

Extremely high concentration of airborne acetone has lethal effects from respiratory failure. In addition, acetone has significant neurological effects and immunological effects. According to most studies, acetone does not impose carcinogenicity and reproductive effects, but some studies showed elevated rate of cancers and reproduction deficiencies at high exposure levels. So because of contradictory data, no IARC, EPA, and U.S. Department of Health and Human Services (DHHS) carcinogenicity category has been located for acetone, and ACGIH lists acetone as “not classifiable as human carcinogen”. Acetone has proven synergistic effects with other contaminants.

There are environmental and biological exposure standards for acetone set up by Canadian and U.S. jurisdictions. Control of acetone exposure includes substitution, engineering control and work practices, and personal protective equipment.

## Part I General Information

### I) Substance name

Acetone

### II) Formula

$(\text{CH}_3)\text{CO}(\text{CH}_3)$

### III) CAS Number

67-64-1

### IV) Synonyms

Dimethylformaldehyde

dimethyl ketone

2-Propanone

Pyroacetic acid

Pyroacetic ether

### V) General Descriptions of Chemical and physical properties

Acetone is a chemical that is found naturally in the environment and is also produced by industries. Low levels of acetone are normally present in the body from the breakdown of fat; the body can use it in normal processes that make sugar and fat [7].

Acetone is a colorless, volatile liquid with a distinct smell and taste [2,7]. People begin to smell acetone in air at 100 to 140 parts of acetone in a million parts of air (ppm), though some can smell it at much lower levels [7]. Acetone is among the most widely used chemicals in industry and commerce. Annual US production exceeds 1 billion kg [2].

Other chemical and physical properties of acetone retrieved from NIOSH guide [1] are summarized in **table 1** as below.

**Table 1 Chemical and Physical Properties of Acetone**

Conversion Factor	1ppm=2.38 mg/m <sup>3</sup>
Boiling Point	56°C (133°F)
Freezing Point	-96°C (-140°F)
Flash Point	-18°C (0°F)
Solubility	Miscible
Vapor Pressure at 20°C	180 mmHg
Ionization Potential	9.69eV
Upper Explosive Limit (UEL)	12.8%
Lower Explosive Limit (LEL)	2.5%
Immediately Dangerous to Life or Health Concentrations (IDLHs)	2500ppm (10% LEL)
Classification of Flammable Liquid	IB (flash point below 73°F and boiling point above 100°F)
Incompatibilities and Reactivities	Oxidizers, acids

## VI) Sampling & Analysis Methods

**Table 2** summarizes standard analysis methods of acetone.

**Table 2 Standard Analysis Methods of Acetone**

Index	Sampling Method	Analytic Method	Limit of Detection	Ref.
US OSHA	Air samples are collected by drawing known volumes of air through standard size sampling tubes containing 130 mg of Carbosieve S-III (carbon based molecular sieve) adsorbent in the front section and 65 mg in the back section.	After sampling, the samples are desorbed with 1% dimethylformamide in carbon disulfide, in the presence of magnesium sulfate, and then analyzed by GC/FID.	LOD: 2.0 ppm	[19]
US NIOSH (Meth. # 1300)	Solid sorbent tube filled with coconut shell charcoal	Desorbed with carbon disulfide and analyzed by GC/FID.	LOD: 0.02 mg/tube	[20]
US NIOSH	Thermal desorption tube containing graphitized carbons and carbon molecular sieve sorbents	Thermally desorbed, then GC/MS	LOD: 100 ng/tube or less	[21]
US NIOSH	Solid sorbent tube containing Anasorb CMS	Desorbed with carbon disulfide and analyzed by GC/FID.	LOD: 900 ng/tube	[22]
US NIOSH	Portable direct-reading instrument	Extractive fourier transform infrared (FTIR) Spectrometry	0.95ppm	[23]

## Part 2 Exposure Among Healthcare Workers

It is estimated that the number of people annually use acetone in occupational settings and consumer products ranges from 3.7 to 112 million [6]. Acetone is used as a chemical intermediate and as a solvent cleaner in fingernail polish remover, paint-related products, and the chemical production of other ketone substances [55].

### I) Exposure routes

#### *Inhalation*

Acetone is rapidly and passively taken up by the respiratory tract and absorbed into the bloodstream during inhalation exposure due to its high blood-air partition coefficient, which ranges from 167 to 330 [7~10]. Human studies showed pulmonary uptakes ranging from 30% to 80% 4 hours after exposure to acetone of 23~4,607 ppm [11~15].

Uptake through inhalation route was proportional to exposure concentration and duration [11]. In addition, inhalation uptake also increased as the level of physical activity increased, i.e., during exercise, due to increased pulmonary ventilation [11, 16]. Lungs (including mouth and trachea) retained a greater percentage of inspired acetone (55%) than the nasal cavity (18%) in humans, indicating that the nasal cavity absorbs acetone less readily than the rest of the respiratory system [12].

#### *Oral*

Measurement of acetone in blood and urine of patients who accidentally or intentionally ingested acetone indicated that acetone was absorbed, but the percentage absorbed cannot be determined from the data. Experiments in rats indicated that acetone is rapidly and almost completely absorbed from the gastrointestinal tract after oral exposure [17].

#### *Dermal*

Dermal absorption of acetone has been demonstrated in humans. Application of cotton soaked in acetone to a 12.5 cm<sup>2</sup> uncovered area of skin of volunteers for 2 hours/day for 4 days resulted in blood levels of acetone of 5~12µg/ml, alveolar air levels of 5~12ppm, and urinary concentrations of 8~14µg/ml on each day [18]. The study also showed that absorption was rapid, with peak blood levels appearing at the end of each daily application.

### II) Monitoring Data

There are 5 monitoring reports of acetone in healthcare settings (hospitals), and all of them were below exposure limit, thus they concluded that acetone is not a potential hazard for healthcare workers [57~61]. Numbers of monitoring results were not given in any of the reports.

There is no individual scientific literature concerning acetone exposure monitoring among healthcare workers.

## Part 3 Metabolism and Pharmacokinetics

### I) Distribution

One study showed that acetone can cross placental barrier and be distributed to breast milk [24]. Acetone level tends to be higher in organs with higher water content because of its high water solubility [25].

### II) Metabolism

The metabolic fate of acetone is independent of route of administration and involves three separate gluconeogenic pathways, with ultimate incorporation of carbon atoms into glucose and other products and substrates of intermediary metabolism with generation of carbon dioxide [25]. The primary (major) pathway involves hepatic metabolism of acetone to acetol and hepatic metabolism of acetol to methylglyoxal, while two secondary (minor) pathways are partially extrahepatic, involving the extrahepatic reduction of acetol to L-1,2-propanediol.

### III) Elimination

Biological half-time for blood elimination has been estimated to be 3~3.9 hours among humans exposed to 100~500 ppm for 2~4 hours [28]. The elimination from blood was found to be complete in 24 hours after a 6-hour exposure in subjects exposed to 250 ppm, in 32 hours in subjects exposed to 500 ppm, and in 48 hours in subjects exposed to 1,000 ppm [29].

### IV) Excretion

The main route of excretion of acetone is via the lungs regardless of the route of exposure. Acetone is excreted both unchanged and, following metabolism, mainly as carbon dioxide [25]. Very little unchanged acetone is excreted in the urine [26,27].

## Part 4 Health Effects

### I) Lethal Effects

#### *Acute*

In animals, high concentrations of acetone may result in respiratory failure and thus produce death. An 8-hour LC<sub>50</sub> value of 21,091 ppm and a 4-hour LC<sub>50</sub> value of 31,994 ppm were found for female rats [32]. In humans, the 1991 Annual Report of the American Association of Poison Control Centers National Data Collection System documented 1,137 incidents of human exposure to acetone without any fatalities [33].

#### *Long-term*

In a retrospective mortality study of 948 employees (697 men, 251 women) of a cellulose fiber plant where acetone was used as the only solvent, no significant excess risk of death from any cause (all causes, malignant neoplasm, circulatory system disease, ischemic heart disease) compared with rates for the U.S. general population [30]. Industrial hygiene surveys found that median time-weighted average acetone concentrations were 380, 770, and 1,070 ppm based on job categories [31].

### II) Irritation

ACGIH TLV for acetone is set up based on the irritation endpoints [52]. Breathing moderate to high levels of acetone for short periods of time can cause nose, throat, lung, and eye irritation [43].

### III) Immunological Effects

Two studies found immunological effects in humans after inhalation exposure to 500ppm acetone for 6 days [29,36], such as significantly increased white blood cell counts, increased eosinophil counts, and decreased phagocytic activity of neutrophils. However, the difference was not significant among volunteers exposed to 250 ppm compared with controls. There is one case report of patchy alopecia areata of a laboratory technician who use acetone as solvent, and following patch testing showed a strong positive reaction [37]. However, generally, acetone sensitization was very rare [25].

### IV) Neurological Effects

Case reports have described patients who became comatose or collapsed after hip casts were applied with acetone present in the setting fluid [34,35]. In another case report, a woman experienced headache, dizziness, weakness, difficulty speaking, and depression after cast containing acetone had been applied [38]. In addition, there are some on-site medical appraisals showing that workers exposed to acetone may develop neurological outcomes. In one appraisal of nine workers who were exposed to TWA acetone of 1006ppm, three of them mentioned headache and lightheadedness as subjective symptoms [39].

Neurological and behavioral effects have also been documented in volunteers tested under controlled laboratory conditions. These effects included general lack of energy and weakness, headache, delayed visual reaction time [29,36]; subjective symptoms of tension, tiredness, complaints and annoyance [40,41]; increases in response and the percent false negatives in auditory discrimination tests and increases in anger and hostility [42]; and increased visual evoked response [43].

Narcotic effects have been observed in animals exposed acutely to high level of acetone vapors (2,000 ~12,000ppm) [44].

## V) Carcinogenicity & Genotoxicity

There has been only one epidemiology study so far concerning the carcinogenicity of acetone: In a retrospective mortality study of 948 employees (697 men, 251 women) of a cellulose fiber plant where acetone was used as the only solvent, no significant excess risk of death from any cause, including malignant neoplasm, was found when compared with rates for the U.S. general population [30,31]. The workers had been employed at the plant for at least 3 months to 23 years. Industrial hygiene surveys found that median time-weighted-average acetone concentrations were 380, 770, and 1,070 ppm, based on job categories.

Currently, there are no animal studies concerning the carcinogenicity of acetone through inhalation or injection route. For the dermal route of exposure, acetone has been used as a solvent for other chemicals in skin painting studies in mice, and as the solvent control in these studies, which suggests that carcinogenic effects through dermal route is negligible [25]. An analysis of the histopathology in female SENCAR mice used as acetone controls in a skin painting study of formaldehyde and held for  $\leq 100$  weeks of age, revealed no neoplastic lesions associated with acetone exposure, that is, any lesions seen were considered spontaneous in this strain [45].

Consequently, because of limited data, no IARC, U.S. Department of Health and Human Services (DHHS), or EPA category has been located for acetone, and ACGIH classified acetone as “A4, not classifiable as human carcinogen”.

Mutagenicity and genotoxicity studies reviewed in the IRIS database have been negative, except for one study which reported chromosomal aberrations [46].

## VI) Reproductive Effects

One laboratory study of volunteers found premature menstrual periods three of four women exposed to 1000 ppm acetone for 7.5 hours, as well as shortening of the menstrual cycle [43]. One epidemiology study among women workers in a Russian factory where workroom levels of acetone ranged from 14 to 126 ppm showed statistically significantly increased incidences of pregnancy complications compared with control group, along with miscarriage, decreased hemoglobin levels, hypotension, and weakness of labor activity [46]. In another epidemiological study of the pregnancy outcome among 556 female laboratory workers, no statistically significant difference in the incidence of miscarriage was found between those exposed to a variety of solvents including acetone and those not exposed to solvents [47].

No effects were observed on the fertility of male Wistar rats treated with drinking water containing acetone at 1,071 mg/kg/day for 6 weeks [48].

## VII) Synergistic Effect with Other Contaminants

The presence of acetone will increase the toxicity of several chemicals, including carbon tetrachloride, chloroform, trichloroethylene, bromodichloromethane, dibromochloromethane, N-nitrosodimethylamine and 1,1,2-trichloroethane, the lung toxicity of styrene and the toxicity of acetonitrile and 2,5-hexanedione in laboratory animals. Mechanism might be that acetone will block the excretion and elimination of ethyl alcohol, which will increase their toxicity [3].



## Part 5 Regulations and Guidelines

### I) Exposure limits

Exposure limits set up by jurisdictions of Canada and U.S. are summarized in **table 3**.

**Table 3 Exposure Limits of Acetone**

	WorkSafeBC	ACGIH	OSHA PEL
TWA <sup>[1]</sup>	250ppm	500ppm	1000ppm
STEL <sup>[2]</sup>	500ppm	750ppm	N/A
Ceiling <sup>[3]</sup>	500ppm	N/A	N/A
BEI <sup>[4]</sup>	N/A	50 mg/L. urine; end of shift; non-specific <sup>[5]</sup> .	N/A
Notations	N/A	BEI; A4 <sup>[5]</sup>	N/A

[1]: 8-hrs time weighted average airborne concentration.

[2]: 15 min short time exposure limit.

[3]: maximum allowable concentration, which may not be exceeded even momentarily.

[4]: biological exposure indices.

[5]: Not classifiable as a human carcinogen.

### II) Hazard Classifications

Hazard classifications of acetone are summarized in **table 4**.

**Table 4 Hazard Classification of Acetone**

Jurisdiction/system	Regulation/Hazard Classification		Ref.
Canadian WHMIS Criteria	<b>B2</b> - Flammable and combustible material - Flammable liquid <b>D2B</b> - Poisonous and infectious material - Other effects - Toxic		[51]
U.S. NIOSH Registry of Toxic Effects of Chemical Substances (RTECS) Number	AL3150000		[1]
U.S. EPA Integrated Risk Information System (IRIS)	Reference Dose (RfD)	0.9 mg·kg <sup>-1</sup> ·day <sup>-1</sup>	[49]
	Reference Concentration (RfC)	N/A, due to lack of data	
NFPA 704 Ratings	Health Hazard Rating <b>1</b> ; Fire Hazard Rating <b>3</b> ; Reactivity Hazard Rating <b>0</b> .		[50]
U.S. Clean Air Act	Acetone is not a hazardous air pollutant (HAP) under the federal Clean Air Act Amendments of 1990.		[50]
U.S. Clean Water Act (CWA)	Acetone is not a priority pollutant under the federal CWA, but its discharge into wastewater would still need to be addressed on a case-by-case basis.		[50]
European Union (EU) Classification and Labelling Information system	It meets the EU criteria for class: <b>F</b> -High flammable		[51]

## Part 6 Control Methods

### I) Substitution

Whenever practical, a substance that gives rise to a harmful atmospheric contaminant should be eliminated or replaced by one with similar technical properties, but which is less harmful to health.

Consideration should be given to the use of water-based, heavy duty detergent cleaners instead of organic solvents, for the removal of dirt and grease on machinery equipment and parts [54]. Where organic solvents are required in a process, investigations of both the technical suitability of the formulation and the health hazards associated with the solvent components are considered essential to determine the product's overall suitability [54].

### II) Engineering and Work Practices

A system of local and/or general exhaust is recommended to keep employee exposures below the airborne exposure limits. Local exhaust ventilation is generally preferred because it can control the emissions of the contaminant at its source, preventing dispersion of it into the general work area [56].

Recommended work practices with acetone are list as below [54].

Avoid manual mixing and pouring by using sealed dispensing units for filling and emptying. This procedure reduces the generation of aerosols and vapors and reduces the opportunities for spillage.

Enclose all cleaning, mixing and pouring procedures where possible. Ensure soaking containers of solvents are fully covered or sealed.

Maintain good hygiene practices. Avoid leaning over solvent- containing vessels, and minimize skin contact and inhalation of vapors. After using solvents, wash gloves prior to removal. Wash hands prior to eating, drinking or using the toilet. Do not eat, drink, or smoke in the workplace.

Degreasing, cleaning or similar operations should be situated in open areas or other locations with good ventilation. Vapors should not be allowed to infiltrate surrounding work areas. This is especially important where naked flames, sparks or welding operations are performed.

### III) Personal Protective Equipment

Canadian Centre for Occupational Health and Safety (CCOHS) recommends wearing suitable personal protective equipment including approved respiratory protection, if engineering controls and work practices are not effective in controlling exposure to acetone, or in case of emergencies such as spills or fire [52].

#### *Respirators*

If respiratory protection is required, then a complete respiratory protection program including selection should be instituted, including fit testing, training, maintenance and inspection [52]. Canadian Standard Association (CSA) Standard Z94.4-93 should be applied. According to NIOSH recommendation [1]: **1**) for airborne acetone level below 2500 ppm, chemical cartridge respirator with organic vapour cartridge(s); or powered air-purifying respirator with organic vapour cartridge(s); or gas mask with organic vapour canister; or supplied-air respirator (SAR); or full-facepiece self-contained

breathing apparatus (SCBA) should be applied. **2)** for emergency or planned entry into unknown concentration or IDLH conditions, positive pressure, full-facepiece SCBA; or positive pressure, full-facepiece supplied-air respirator (SAR) with an auxiliary positive pressure self-contained breathing apparatus (SCBA) should be applied.

### ***Skin Protection***

CCOHS recommends that chemical resistant gloves, coveralls, boots, etc., can be applied to prevent prolonged or repeated contact. Recommended types of materials that protective clothing can be made of are butyl rubber, Teflon (TM), 4H (TM), Barricade (TM), Chemrel (TM), Responder (TM), as the resistance to breakthrough is longer than 8 hours [53]. Materials not recommended are natural rubber, neoprene, nitrile rubber, polyethylene, polyvinyl alcohol, polyvinyl chloride, Viton (TM), Saranex (TM), as the resistance to breakthrough is less than 1 hour.

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