Appendix A

OECD SIDS Dossier and SIAR for Acetone

H E D S E T

D a t a S h e e t

CAS-No.:	67-64-1
EINECS-No.:	200-662-2
IUPAC-Name:	Acetone

1.03 Submitter Identification

Company	Environmental Protection Agency
Street	401 M Street, SW
Date	02/20/97
Postal Code	20460
Town	Washington, DC
Country	United States
Phone	202-260-3749
Telefax	202-260-8168
Telex	N/A

1.04 OECD and Company Information

Type	lead organization
Name	Environmental Protection Agency
Partner	Chemical Manufacturers Association
Date	02/20/97
Street	401 M Street, SW
Postal Code	20460
Town	Washington DC
Country	United States
Phone	202-260-3749
Telefax	202-260-8168
Telex	N/A
Other Manufacturer	no

1.1 Substance Information

Molecular Formula:	C3H6O
Molecular Weight:	58.08
Smiles Code:	CC(=O)C
Substance Type	organic
Physical Status	liquid
Purity	99.5-99.8% (w/w)

1.2 Synonyms

Remark	2-Propanone Beta-Ketopropane Acetone Dimethyl Ketone Methyl Ketone Propanone Ketone Propane Ketone, Dimethyl

1.3 Impurities

Remark	Water, not more than 0.5 wt % (ASTM D1364); acidity (as free acetic acid), not more than 0.002 wt %, equivalent to 0.019 mg of KOH per gram of sample (ASTM D1613); water miscibility, no turbidity or cloudiness at 1:10 dilution with water (ASTM D1722); alkalinity (as ammonia), not more than 0.001 wt % (ASTM D1614); and permangamate time, color of added $KMnO_4$ must be retained at least 30 min at 25 °C in the dark (ASTM D1363).
Remark	Other impurities that have been identified include: benzene (0-50 ppm), acetaldehyde (0-70 ppm), methanol (0-500 ppm), diacetone alcohol (0-300 ppm), mesityl oxide (0-10 ppm), formaldehyde (0-1 ppm), isopropanol (0-100 ppm).
Reference	Kirk-Othmer. 1991. Encyclopedia of Chemical Technology, Fourth Edition. Volume 1. John Wiley & Sons. New York. Gerlich, O. (1995). Euclid data sheet: Acetone. Existing Substance Dossier. Phenolchemie GmbH. Gladbeck, Germany.

1.5 Quantity

Quantity Produced or Imported	>1,000,000 tons (1993)
Produced 12 mo After Regulation	yes
Imported 12 mo After Regulation	yes
Remark	11 Producers in United States, global production.
Information Source	Chemical Manufacturers Association

1.6.1 Labelling

Labelling	As in Directive 67/548/EEC
Specific Limits	no
Symbols F	Nota
R Phrases	11
S Phrases	9-16-23-33
Text	Keep container in a well-ventilated place--Keep away from sources of ignition--No smoking--Do not breathe vapors--Take precautionary measures against static discharges. Separate the phrases with '-' and the text for S-phrases with '--'.

1.6.2 Classification

Classification	as in Directive 67/548/EEC
Class of Danger	highly flammable
R Phrases	11

1.7 Use Pattern

Type	industrial
Category	chemical industry: used in synthesis
Remark	bisphenol-A, isophorone, methyl isobutyl ketone, other chemical intermediates

Type	industrial
Category	basic industry: basic chemicals
Remark	major use as solvent for fats, oils, waxes, resins, plastics, lacquers, paints, inks, varnishes, rubber cements

Type	industrial
Category	chemical industry: used in synthesis
Remark	methyl methacrylate, methacrylic acid and higher methacrylates (33%)

Type	industrial
Category	process solvent: used in manufacturing
Remark	smokeless gunpowder, cellulose acetate yarn, vitamin intermediates

Type	industrial
Category	other
Remark	antiseptic solution, cleaning and drying agent, pharmaceutical aid

1.8 Occupational Exposure Limit Values

Type of Limit	8-h TWA PEL (OSHA)
Value	2400 mg/m^3 (1000 ppm)
Country	United States
Reference	Code of Federal Regulations 41:50-204.50, 1994.

Type of Limit	8-h TWA
Value	1185 mg/m^3 (500 ppm)
Country	Australia
Remark	Short-Term Exposure Limit 2400 mg/m^3 (1000 ppm)

Type of Limit	8-h MAK (DE)
Value	1200 mg/m^3 (500 ppm)
Country	Austria, Germany, Switzerland (DFG-MAK/DFG-Peak)
Remark	Short-Term Exposure Limit 6000 mg/m^3 (2500 ppm)

Type of Limit	8-h TWA TLV
Value	1780 mg/m^3 (750 ppm)
Country	Belgium, Luxembourg: ARAB-TWA/ARAB-STEL Ireland, Italy: ACGIH-TWA/ACGIH-STEL Portugal, Spain: ACGIH-TWA/ACGIH-STEL
Remark	Short-Term Exposure Limit 2400 mg/m^3 (1000 ppm)

Type of Limit	8-h TWA OEL
Value	800 mg/m^3 (330 ppm)
Country	Czechoslovakia
Remark	Short-Term Exposure Limit 4000 mg/m^3 (1660 ppm)

Type of Limit	8-h TWA (AGSM)
Value	600 mg/m^3 (250 ppm)
Country	Denmark

Type of Limit	8-h TWA
Value	200 mg/m^3 (84 ppm)
Country	China

Type of Limit	8-h TWA OEL
Value	1200 mg/m^3 (500 ppm)
Country	Finland
Remark	Short Term Exposure Limit 1500 mg/m^3 (625 ppm)

Type of Limit	8-h TWA OEL
Value	1800 mg/m^3 (750 ppm)
Country	France

Type of Limit	8-h TWA OEL
Value	600 mg/m^3 (250 ppm)
Country	Hungary
Remark	Short Term Exposure Limit 1200 mg/m^3 (500 ppm)

Type of Limit	8-h TWA OEL
Value	1780 mg/m^3 (750 ppm)
Country	India
Remark	Short Term Exposure Limit 2375 mg/m^3 (1000 ppm)

Type of Limit	MAC (Japan)
Value	470 mg/m^3 (200 ppm)
Country	Japan

Type of Limit	MAC (NL) 8-h TWA
Value	1780 mg/m^3 (750 ppm)
Country	The Netherlands

Type of Limit	8-h TWA OEL
Value	2400 mg/m^3 (1000 ppm)
Country	The Philippines

Type of Limit	8-h TWA OEL
Value	200 mg/m^3 (84 ppm)
Country	Poland

Type of Limit	8-h TWA
Value	200 mg/m^3 (84 ppm)
Country	Russia
Remark	Short Term Exposure Limit 200 mg/m^3 (84 ppm)

Type of Limit	8-h TWA OEL
Value	600 mg/m^3 (250 ppm)
Country	Sweden
Remark	Short Term Exposure Limit 1200 mg/m^3 (500 ppm)

Type of Limit	8-h TWA OEL
Value	2400 mg/m^3 (1000 ppm)
Country	Turkey

Type of Limit	8-h TWA (EH40)
Value	1780 mg/m^3 (750 ppm)
Country	United Kingdom
Remark	Short Term Exposure Limit 3560 mg/m^3 (1500 ppm)

Type of Limit	8-h TLV TWA (ACGIH)
Value	1780 mg/m^3 (750 ppm)
Country	United States
Remark	Short-Term Exposure Limit 2375 mg/m^3 (1000 ppm)
Remark	Exposures above the TLV-TWA up to the STEL should not be longer than 15 minutes and should not occur more than four times per day.

1.9 Source of Exposure

Remark	Acetone is a product of the photooxidation of some alkane and alkene compounds that are found in urban air and is also a by-product resulting from oxidation of humic substances. In addition, natural sources of acetone include by-products from forest fires, volcanoes, and metabolism of insects and higher animals.
Remark	Acetone is a normal constituent of human blood and is a component of human breath (of metabolic origin).
Remark	Acetone may be released to the environment as stack emissions, fugitive emissions, and in waste water in its production and use in the manufacture of methacrylates, as

a solvent, and as a chemical intermediate in the manufacture of methyl isobutyl ketone and other chemicals.

Remark: Acetone has also been identified in wastewater from industrial and municipal treatment plants.

Remark: Acetone does not appear to be persistent in the environment due to its biodegradability, despite its widespread presence in the environment.

2. Physico-chemical Data

2.1 Melting Point

Value	-94.6 °C
GLP	no data
Reference	Handbook of Chemistry and Physics (1986). R.C. Weast (ed.), 67th Ed., p. C51. CRC Press Inc. Boca Raton, FL.

2.2 Boiling Point

Value	56.1 °C at 760 mm Hg
GLP	no data
Reference	Handbook of Chemistry and Physics (1986). R.C. Weast (ed.), 67th Ed., p. C51. CRC Press Inc. Boca Raton, FL.

2.3 Density

Value	0.791 g/mL at 20 °C
GLP	no data
Reference	Handbook of Chemistry and Physics (1986). R.C. Weast (ed.), 67th Ed., p. C51. CRC Press Inc. Boca Raton, FL.

2.4 Vapour Pressure

Value	182 mm Hg at 20 °C
GLP	no data
Reference	Kirk-Othmer Encyclopedia of Chemical Technology (1991). 4th Ed. Volume 1. John Wiley & Sons, New York, NY.

Value	230 mm Hg at 25 °C

Method	other (calculated)
GLP	no data
Reference	NOMO5 Program. Syracuse Research Corp.,Syracuse, NY.

2.5 Partition Coefficient

Value	-0.24
Type	Log P_{ow}
GLP	no
Reference	Hansch, C. and Leo, A. (1979). Substituent Constants for Correlation Analysis in Chemistry and Biology, p. 179. John Wiley & Sons, New York, NY.

2.6 Water Solubility

Description	miscible
GLP	no data
Remark	Miscible with water, alcohol, dimethylformamide, ether.
Reference	The Merck Index (1983). M. Windholz (ed.), 10th Ed., p. 57. Merck & Co., Rahway, NJ.

2.7 Flash Point

Value	-17 °C
Type	closed cup
GLP	no data
Reference	Fire Hazard Properties of Flammable Liquids, Gases, and Volatile Solids (1991). National Fire Protection Association, NFPA 325M, 10th Ed. Quincy, MA.

2.8 Auto Flammability

Value	465 °C (autoignition temperature)
GLP	no data
Reference	Fire Hazard Properties of Flammable Liquids, Gases, and Volatile Solids (1991). National Fire Protection Association, NFPA 325M, 10th Ed. Quincy, MA.

2.9 Flammability

Result	highly flammable
GLP	no data
Reference	Fire Hazard Properties of Flammable Liquids, Gases, and

Volatile Solids (1991). National Fire Protection Association, NFPA 325M, 10th Ed. Quincy, MA.

2.10 Explosive Properties

Result	not explosive
GLP	no data
Reference	Fire Hazard Properties of Flammable Liquids, Gases, and Volatile Solids (1991). National Fire Protection Association, NFPA 325M, 10th Ed. Quincy, MA.

3. Environmental Fate and Pathways

3.1 Stability

3.1.1 Photodegradation

Type	air
Light Source	xenon lamp
Light Spect.	250-330 nm
Rel. Intens.	Based on intensity of sunlight
Spectrum	lambda (max) >295 nm epsilon (max) 295 nm
Concentration	200 mg/L
GLP	no data
Test substance	no data
Result	Quantum yield varied with wavelength from 1.59 to 0.27 for CO_2 production. Direct photolysis half-life was 32 days. The half-life reported is the annual average in the lower troposphere at 40 degrees northern latitude. Indirect photolysis rate constant estimated to be 0.00000026 cm^3/mol/sec based on OH sensitizer concentration of 1,180,000 mol/cm^3.
Test condition	Temperature for direct photolysis test equaled room temperature
Reference	Meyrahn, H., Pauly, J., Schneider, W., and Warneck, P. (1986). Quantum yields for the photodissociation of acetone in air and an estimate for the lifetime of acetone in the lower troposphere. J. Atmos. Chem. 4:277-291.

Type	air
Light Spect.	279-313 nm
Rel. Intensity	based on intensity of sunlight

Spectrum	lambda (max) >295 nm epsilon (max) 295 nm
GLP	no data
Test substance	no data
Result	Quantum yield: 0.15 (25 torr); 0.08 (> 400 torr) Photolysis half-life is 40 days near the earth surface to 10 days at 200 mbar pressure. Attack by hydroxyl radicals with half-life of 20 days near earth surface to 100 days at 200 mbar pressure.
Reference	Gardner, E.P. (1984). The primary quantum yields of photodecomposition of acetone in air under tropospheric conditions. J. Phys. Chem. 88:5069-5076. Chatfield, R.B., Gardner, E.P., and Calvert, J.G. (1987). Sources and sinks of acetone in the troposphere: Behavior of reactive hydrocarbons and a stable product. J. Geophys. Res. 92:4208-4216.

3.2 Monitoring Data (Environment)

Type	background concentration
Media	air
Remark	Acetone detected at 1.6-4 part per billion by volume (ppbv), 4.8-12 ppbC, average concentration over a 1-yr period in Denver, Colorado, USA.
Reference	Anderson, L.G., Lanning, J.A., and Wolfe, P. (1994). Acetone in the urban atmosphere: A case study in Denver, Colorado. Israel J. Chem. 34:341-353.

Type	background concentration
Media	air
Remark	1.6 ppb (4.8 ppbC) and 1.8 ppb (5.4 ppbC) found in two rural sites in Ontario, Canada, 1988.
Reference	Shepson, P.B., Hastie, D.R., Schiff, H.I., Polizzi, M., Bottenheim, J.W., Anlauf, K., Mackay, G.I., and Karecki, D.R. (1991). Atmospheric concentrations and temporal variations of C_1-C_3 carbonyl compounds at two rural sites in central Ontario. Atmos. Environ. 25A:2001-2015.

Type	background concentration
Media	air
Remark	12 ppb (36 ppbC) in troposphere above Tucson, Arizona; 2.8 ppb (8.4 ppbC) at two rural sites 40 km away.

Reference	Snider, J.R. and Dawson, G.A. (1985). Tropospheric light alcohols, carbonyls, and acetonitrile: Concentrations in the southwestern United States and Henry's Law data. J. Geophys. Res. 90:3797-3805.
Type	background concentration
Media	air
Remark	Range of 4.1-94 part per billion by volume (ppbv), 12.3-282 ppbC, at two urban sites in USA. Additionally, a range of 19.5-89.6 ppbv, (58.5-268.8 ppbC) was reported in a variety of work settings, including indoor air.
Reference	Kelly, T.J., Callahan, P.J., Piell, J., and Evans, G.F. (1993). Method development and field measurements for polar volatile organic compounds in ambient air. Environ. Sci. Technol. 27:1146-1153.
Type	background concentration
Media	air
Remark	Qualitative detection in volcanic gas from Guatemala.
Reference	Stoiber, R.E., Leggett, R.E., Jenkins, T.F., Murrmann, R.P., and Rose, W.I. (1971). Organic compounds in volcanic gas from Santiaguito volcano, Guatemala. Am. Geolog. Soc. Bull. 82:2299-2302.
Type	contaminated site
Media	air
Remark	Acetone detected at 770-4100 parts per billion by volume (ppbv) 2310-12,300 ppbC, around several different manufacturing sites.
Reference	Hoshitia, Y., Nihei, Y., Muto, G. (1981). Pattern display for characterization of trace amounts of odorants discharged from nine odor sources. Analyst 106:1187-1202.
Type	background concentration
Media	air
Remark	6.7-32.3 parts per billion as carbon (ppbC) was detected in seven Florida (USA) sites.
Reference	Lonneman, W.E., Sella, R.L., and Bufalini, J.J. (1978). Ambient air hydrocarbon concentrations in Florida. Env. Sci. Technol. 12:459-463.
Type	background concentration

Media	air
Remark	0.5-20.6 parts per billion as carbon (ppbC) was detected in USA continental and marine areas.
Reference	Duce, R.A., Mohnen, V.A., Zimmerman, P.R., Grosjean, D., Cautreels, W., Chatfield, R., Jaenicke, R., Ogren, J.A., Pelliari, E.D., and Wallace, G.T. (1983). Organic material in the global troposphere. Rev. Geophys. Space Phys. 21:921-952.

Type	background concentration
Media	air
Remark	An average of 470 parts per trillion by volume (pptv) (1410 pptC) of acetone at ground level to 120 pptv (360 pptC) in the upper troposphere was detected.
Reference	Arnold, F., Knop, G., and Ziereis, H. (1986). Acetone measurements in the upper troposphere and lower stratosphere- implications for hydroxyl radical abundances. Nature 321:505-507.

Type	background concentration
Media	air
Remark	4-52 part per billion as carbon (ppbC) was detected at three sites in the USA.
Reference	Arnts, R.R. and Meeks, S.A. (1981). Biogenic hydrocarbon contribution to the ambient air of selected areas. Atmos. Environ. 15:1643-1651.

Type	contaminated site
Media	ground water
Remark	A concentration of 43,700 μg/L was detected onsite at a contaminated landfill; 0.2-0.7 μg/L acetone was found in wells adjacent to the landfill.
Reference	DeWalle, F.B. and Chien, E.S.K. (1981). Detection of trace organics in well water near a solid waste landfill. J. Am. Water Works Assoc. 73:206-211.

Type	contaminated site
Media	air
Remark	20-250 part per billion by volume (ppbv) (60-750 ppbC) was detected in a house near a contaminated landfill.
Reference	Hodgson, A.T., Garbesi, K., Sextro, R.G., and Daisey, J.M. (1992). Soil-gas contamination and entry of volatile organic compounds into a house near a landfill. J. Air

Waste Manage. Assoc. 42:277-283.

Type	other
Media	air
Remark	Acetone was detected in seven different product categories. The percentage of products with acetone at the average concentration (w/w%) are as follows: 23% automotive - 28.1 11% household cleaners - 0.3 51% paints - 29.3 15% fabric & leather - 12.9 16% electronic equipment - 0.3 5% oils, greases, lubricants - 0.2 24% adhesives - 18.8
Reference	Sack, T.M., Steele, D.H., Hammerstrom, K., and Remmers, J. (1992). A survey of household products for volatile organic compounds. Atmos. Environ. 26A:1063-1070.

Type	other
Media	air
Remark	Acetone was found in the homes of smoking and non-smoking adults at average concentrations of 71 and 50 $\mu g/m^3$, respectively.
Reference	Heavner, D.L., Morgan, W.T., and Ogden, M.W. (1996). Determination of volatile organic compounds and respirable suspended particulate matter in New Jersey and Pennsylvania homes and workplaces. Environ. Int. 22:159-183.

Type	other
Media	air
Remark	Acetone was emitted from particle board at rate ranging from 37- 41 $\mu g/m^2/h$.
Reference	Tichenor, B.A. and Mason, M.A. (1988). Organic emissions from consumer products and building materials to the indoor environment. J. Air Pollut Control Assoc. 38:264-268.

Type	other
Media	air
Remark	78.8 ppm (236.4 ppmC) found in smoke from polypropylene burning.
Reference	Woolley, W.D. (1982). Smoke and toxic gas production

from burning polymers. J. Macromol. Sci. Chem. A17:1-33.

Type	background concentration
Media	air
Remark	14-66 μg/m^3 (6-30 ppb) (18-120 ppbC) acetone was detected in a new office building over a period of one year.
Reference	Hodgson, A.T., Daisey, J.M., and Grot, R.A. (1991). Sources and source strengths of volatile organic compounds in a new office building. J. Air Waste Manage. Assoc. 41:1461-1468.

Type	contaminated site
Media	air
Remark	6838-32,500 part per billion by volume (ppbv) (20,514-97,500 ppbC) was detected in the air at municipal landfill sites.
Reference	Brosseau, J. and Heitz, M. (1994). Trace gas compound emissions from municipal landfill sanitary sites. Atmos. Environ. 28:285-293.

Type	contaminated site
Media	water
Remark	Acetone ranged from 9 ppb influent to 41 ppb effluent in a textile finishing plant.
Reference	Gordon, A.W. and Gordon, M. (1981). Analysis of volatile organic compounds in a textile finishing plant effluent. Trans. Ky. Acad. Sci. 42:149-157.

Type	background concentration
Media	water
Remark	0-41 ng/mL acetone was detected in cloud water at a remote continental (USA) site.
Reference	Aneja, V.P. (1993). Organic compounds in cloud water and their deposition at a remote continental site. J. Air Waste Manage. Assoc. 43:1239-1244.

Type	background concentration
Media	water
Remark	0-0.052 mg/L acetone was detected in seawater samples from Florida and the Eastern Mediterranean.
Reference	Corwin, J.F. (1969). Volatile oxygen-containing organic compounds in sea water: Determination. Bull. Marine Sci.

19:504-509.

Type	background concentration
Media	biota
Remark	Acetone is a normal endogenous biochemical that can be routinely detected and measured in body fluids. Detectable amounts of acetone have been found in a variety of biological specimens including whole blood (fetal through adult), cerebrospinal fluid, urine, exhaled air, and breast milk.
Reference	Dowty, B.J., Laseter, J.L., and Storer, J. (1976). The transplacental migration and accumulation in blood of volatile organic compounds. Pediatr. Res. 10:696-701. Sulway, M.J., Trotter, M.D., Trotter, E., and Malins, J.M. (1971). Acetone in uncontrolled diabetes. Postgrad. Med. J. 47(Suppl.):383-387. Zlatkis, A., Bertsch, W., Lichtenstein, H.A., Tishbee, A., Shunbo, F., Liebich, H.M., Coscia, A.M., and Fleischer, N. (1973). Profile of volatile metabolites in urine by gas chromatography-mass chromatography. Anal. Chem. 45:763-767. Pellizzari, E.D., Hartwell, T.D., Harris, B.S.H., Waddell, R.D., Whitaker, D.A., and Erickson, M.D. (1982). Purgeable organic compounds in mother's milk. Bull. Environ. Contam. Toxicol. 28:322-328.

Type	background concentration
Media	biota
Remark	The normal limit for blood, serum, and plasma acetone in non-fasting adults has been shown to range from 0.8-4.4 mg/L depending on the analytical method applied. The acetone concentration in plasma can be 8-11% greater than the level in whole blood. Infants, pregnant women, and training athletes can have ketone body levels that are elevated 2 to 20-fold above normal due to the ketogenesis resulting from their higher energy requirements.
Reference	Paterson, P., Sheath, J., Taft, P., and Wood, C. (1967). Maternal and foetal ketone concentration in plasma and urine. Lancet II:862-865.

Koeslag, J.H., Noakes, T.D., and Sloan, A.W. (1980). Post-exercise ketosis. J. Physiol. 301:79-90.

Ashley, D.L., Bonin, M.A., Cardinali, F.L. McCraw, J.M., and Wooten, J.V. (1994). Blood concentrations of volatile organic compounds in a nonoccupationally exposed US population and in groups with suspected exposure. Clin. Chem. 40:1401-1404.

Trotter, M.D., Sulway, M.J., and Trotter, E. (1971). The rapid determination of acetone in breath and plasma. Clin. Chem. Acta 35:137-143.

Kimura, M., Kobayashi, K., Matsuoka, A., Hayashi, K., and Kimura, Y. (1985). Head-space gas-chromatographic determination of 3-hydroxybutyrate in plasma after enzymic reactions, and the relationship among the three ketone bodies. Clin. Chem. 31:596-598.

Brega, A., Villa, P., Quadrini, G., Quadri, A., and Lucarelli, C. (1991). High-performance liquid chromotographic determination of acetone in blood and urine in the clinical diagnostic laboratory. J. Chromatogr. 553:249-254.

Gavino, V.C., Vinet, B., David, F, Garneau, M., and Brunengraber, H. (1986). Determination of the concentration and specific activity of acetone in biological fluids. Anal. Biochem. 152:256-261.

Wang, G., Maranelli, G., Perbellini, L., Raineri, E., and Brugnone, F. (1994). Blood acetone concentration in "normal people" and in exposed workers 16 h after the end of the workshift. Int. Arch. Occup. Environ. Health65:285-289.

Type	background concentration
Media	biota
Remark	Endogenous acetone concentrations in normal human spot urine specimens have been shown to range from 0.3-3.0 mg/L. The urinary concentration of acetone was not found to increase appreciably when test subjects performed light physical exercise. A consistent diurnal trend was

observed, however, with higher urine acetone concentrations found in the late evening and early morning than during the day.

Reference

Brega, A., Villa, P., Quadrini, G., Quadri, A., and Lucarelli, C. (1991). High-performance liquid chromatographic determination of acetone in blood and urine in the clinical diagnostic laboratory. J. Chromatogr. 553:249-254.

Kobayashi, K., Okada, M., Yasuda, Y., and Kawai, S. (1983). A gas chromatographic method for the determination of acetone and acetoacetic acid in urine. Clin. Chem. Acta 133:223-226.

Levey, S., Balchum, O.J., Medrano, V., and Jung, R. (1964). Studies of metabolic products in expired air. II. Acetone. J. Lab. Clin. Med. 63:574-584.

Pezzagno, G., Imbriani, M., Ghittori, S., and Capodaglio, E. (1988). Urinary concentration, environ-mental concentration, and respiratory uptake of some solvents: Effect of the work load. Am. Ind. Hyg. Assoc. J. 49:546-552.

Wang, G., Maranelli, G., Perbellini, L., Raineri, E., and Brugnone, F. (1994). Blood acetone concentration in "normal people" and in exposed workers 16 h after the end of the workshift. Int. Arch. Occup. Environ. Health 65:285-289.

Type: background concentration

Media: biota

Remark: The normal value for endogenous acetone in expired air specimens from adult humans was found to average between 0.7-1.6 mg/L, regardless of whether the subjects were fed or fasted overnight.

Reference

Rooth, G. and Tibbling, G. (1968). Free fatty acids, glycerol and alveolar acetone in obese women during phenformin treatment. Acta Med. Scand. 184:263-267.

Rooth, G. and Östenson, S. (1966). Acetone in alveolar air, and the control of diabetes. Lancet II:1102-1105.

Levey, S., Balchum, O.J., Medrano, V., and Jung, R. (1964). Studies of metabolic products in expired air. II. Acetone. J. Lab. Clin. Med. 63:574-584.

Crofford, O.B., Mallard, R.E., Winton, R.E., Rogers, N.L., Jackson, J.C., and Keller, U. (1977). Acetone in breath and blood. Trans. Am. Clin. Climatol. Assoc. 88:128-139.

Trotter, M.D., Sulway, M.J., and Trotter, E. (1971). The rapid determination of acetone in breath and plasma. Clin. Chem. Acta 35:137-143.

Jansson, B.O. and Larsson, B.T. (1969). Analysis of organic compounds in human breath by gas chromatography-mass spectrometry. J. Lab. Clin. Med. 74:961-966.

Stewart, R.D. and Boettner, E.A. (1964). Expired-air acetone in diabetes mellitus. New Eng. J. Med. 270:1035-1038.

Tassopoulos, C.N., Barnett, D., and Fraser, T.R. (1969) Breath-acetone and blood-sugar measurements in diabetes. Lancet II:1282-1286.

Phillips, M. and Greenberg, J. (1987). Detection of endogenous acetone in normal human breath. J. Chromatogr. 422:235-238.

Wang, G., Maranelli, G., Perbellini, L., Raineri, E., and Brugnone, F. (1994). Blood acetone concentration in "normal people" and in exposed workers 16 h after the end of the workshift. Int. Arch. Occup. Environ. Health 65:285-289.

Type	other
Media	biota
Remark	Four workers exposed to 30 ppm (71.1 mg/m^3) of acetone for 2 h were found to retain about 80% of the inhaled acetone. The concentration of acetone in the urine increased from about 0.75 mg/L at the beginning of the workshift to about 2.0 mg/L by the end of the shift. The acetone in venous blood increased from 1.0 mg/L at the

	start of the shift to 3.3 mg/L by the end. Urine and blood acetone levels returned to normal within 24 h.
Reference	Baumann, K. and Angerer, J. (1979). Untersuchungen zur Frage der beruflichen Lösungsmittelbelastung mit Aceton. Krebsgefaehrdung Arbeitsplatz Arbeitsmed. 19:403-408.

Type	other
Media	biota
Remark	Biological monitoring of styrene exposure in the workplace was not affected by co-exposures to acetone. Styrene metabolite concentrations in the urine of 22 workers exposed to styrene and acetone were not affected by 8-h TWA acetone exposures that ranged from about 10-210 ppm (25 to 498 mg/m^3).
Reference	DeRosa, E., Cellini, M., Sessa, G., Saletti, C., Rausa, G., Marcuzzo, G., and Bartolucci, G.B. (1993). Bio-logical monitoring of workers exposed to styrene and acetone. Int. Arch. Occup. Environ. Health 65:S107-S110.

3.3 Transport and Distribution in Environmental Compartments

3.3.1 Transport

Type	volatility
Media	water-air
Method	mass-transfer coefficients measurement
Result	The liquid film mass-transfer coefficient K_L ranged from 0.28-0.54 m/day.
Reference	Rathbun, R.E. and Tai, D.Y. (1982). Volatilization of ketones from water. Water Air Soil Pollut. 17:281-293.

Type	volatility
Media	water-air
Method	acetone measured in model stream
Result	Volatilization coefficient ranged from 82,300-111,000 min^{-1}.
Reference	Rathbun, R.E., Stephans, D.W., and Tai, D.Y. (1991). Fate of acetone in an outdoor model stream with a nitrate supplement, southern Mississippi, U.S.A. J. Hydrol. 123:225-242.

3.3.2 Distribution

Media	water-air
Method	other (measurement)
Remark	Partition between air and seawater at a variety of temperatures was measured and calculated.
Result	Partition coefficient K (m/atm) was 14.8-71.3.
Reference	Zhou, X. and Mopper, K. (1990). Apparent partition coefficients of 15 carbonyl compounds between air and seawater and between air and freshwater: Implications for air-sea exchange. Environ. Sci. Technol. 24:1864-1869.

Media	water sediment
Method	other (measurement)
Result	200-230 ppm acetone was detected in wastewater; acetone was not detected in river water or sediment.
Reference	Jungclaus, G.A., Lopez-Avila, V., and Hites, R.A. (1978). Organic compounds in an industrial wastewater: A case study of their environmental impact. Environ. Sci. Technol.12:88-96.

Media	water-air
Method	other (measurement)
Result	Henry's law constant was 25.6-27.0 m/atm at 25°C.
Reference	Betterton, E.A. (1991). The partitioning of ketones between the gas and aqueous phases. Atmos. Environ. 25A:1473-1477.

3.4 Mode of Degradation

Remark	biological oxidation
Reference	Rathbun, R.E., Stephens, D.W., and Tai, D.Y. (1993). Bacterial degradation of acetone in an outdoor model stream. Environ. Pollut. 79,153-162. Rathbun, R.E., Stephans, D.W., and Tai, D.Y. (1991). Fate of acetone in an outdoor model stream with a nitrate supplement, southern Mississippi, U.S.A. J. Hydrol. 123,225-242. Taylor, D.G., Trudgill, P.W., Cripps, R.E., and Harris, P.R. (1980). The microbial metabolism of acetone. J. Gen. Microbiol. 118,159-170.

3.5 Biodegradation

Type	aerobic
Inoculum	activated sludge, domestic
Degradation	78% after 28 days
Results	readily biodegradable
Method	OECD Guideline 301 D
GLP	no data
Test substance	no data
Reference	Waggy, G.T., Conway, R.A., Hansen, J.L., and Lessing, R.L. (1994). Comparison of 20-d BOD and OECD closed-bottle biodegradation tests. Environ. Toxicol. Chem. 13:1277-1280.

Type	aerobic
Inoculum	activated sludge, domestic
Concentration	100 mg/L
Degradation	42% after 155 h
Method	other
GLP	no data
Test substance	no data
Reference	Urano, K. and Kato, Z. (1986). A method to classify biodegradabilities of organic compounds. J. Hazard. Materials 3:147-159.

Type	aerobic
Inoculum	activated sludge, domestic
Concentration	500 mg/L
Degradation	0% after 24 h
Results	Under test conditions no biodegradation observed
Method	other
GLP	no
Test substance	no data
Remark	This study used a quite high substrate concentration for a limited period of time (24 h), when contrasted to more current methods.
Reference	Gerhold, R.M. and Malaney, G.W. (1966). Structural determinants in the oxidation of aliphatic compounds by activated sludge. J. Water Pollut. Control Fed. 38:562-579.

Type	aerobic
Inoculum	activated sludge, domestic
Concentration	2.5 mg/L
Degradation	78.2%

Results	readily biodegradable
Method	other
GLP	no
Test substance	no data
Remark	Results based on BOD.
Reference	Lamb, C.B. and Jenkins, G.F. (1952). B.O.D. of synthetic organic chemicals. Proc. Ind. Waste Conf. 36:326-339.

Type	aerobic
Inoculum	activated sludge, domestic, adapted
Concentration	333 mg/L
Degradation	86% after 8 h
Results	readily biodegradable
Method	other
GLP	no
Test substance	no data
Reference	Hatfield, R. (1957). Biological oxidation of some organic compounds. Ind. Eng. Chem. 49:192.

Type	aerobic
Inoculum	activated sludge, domestic, adapted
Degradation	47% after 10 days
Method	other
GLP	no
Test substance	no data
Remark	Early study of a wastewater treatment plant.
Test concentration	250-1000 mg/L.
Reference	Mills, E.J. and Stack, V.T. (1954). Biological oxidation of synthetic organic chemicals. Proc. Ind. Waste. Conf. 38:492-517.

Type	aerobic
Inoculum	activated sludge, domestic, adapted
Degradation	38% after 5 days
GLP	no data
Test substance	no data
Remark	Results based on BOD measurement.
Test concentration	0.4-3.2 mg/L
Reference	Babeu, L. and Vaishnav, D.D. (1987). Prediction of biodegradability for selected organic chemicals. J. Ind. Microbiol. 2:107-115.

Type	anaerobic

Inoculum	inoculum from sediment and groundwater
Concentration	50 mg/L
Degradation	100% after 244 days
GLP	no data
Test substance	no data
Remark	Test concentration reported as ppm carbon.
Remark	Results were comparable in sulfite and nitrate-reducing systems.
Reference	Mormile, M.R., Liu, S., and Suflita, J.M. (1994). Anaerobic biodegradation of gasoline oxygenates: Extrapolation of information to multiple sites and redox conditions. Environ. Sci. Technol. 28:1727-1732.

Type	aerobic
Inoculum	activated sludge, domestic
Concentration	10 mg/L
Degradation	81% after 20 days
GLP	no data
Test substance	no data
Remark	BOD/ThOD ratio.
Reference	Young, R.H.F., Ryckman, D.W., and Buzzell, J.C. (1968). An improved tool for measuring biodegradability. J. Water Pollut. Control Fed. 40:R354-R368.

Type	aerobic
Inoculum	activated sludge, domestic
Concentration	3.2 mg/L
Degradation	38% after 5 days
GLP	no data
Test substance	no data
Remark	results based on BOD.
Reference	Vaishnav, D.D., Boethling, R.S., and Babeu, L. (1987). Quantitative structure-biodegradability relationships for alcohols, ketones and alicyclic compounds. Chemosphere 16:695-703.

Type	aerobic
Inoculum	lab-generated organisms seeded from domestic sludge.
Degradation	100%
GLP	no data
Test substance	no data
Remark	Removal rate was 125 mg/L/day after a 5-day lag.
Concentration	166-500 mg/L.

Reference	Chou, W.L., Speece, R.E., and Siddiqi, R.H. (1978). Acclimation and degradation of petrochemical wastewater components by methane fermentation. In: Biotechnology and Bioengineering Symposium No. 8., C.D. Scott, ed., pp. 391-414. John Wiley and Sons, New York, NY.

3.6 BOD_5, COD or BOD_5/COD Ratio

Method	other
Year	1979
BOD_5	1.85 g/g
COD	1.92 g/g
GLP	no data
BOD_5/COD Ratio	0.96
Method	APHA "Standard Methods" 1989.
Concentrations	3, 7, and 10 mg/L were used.
Remark	In additional testing, BOD_{10}, BOD_{15}, and BOD_{20} were determined (Birdie et. al., 1979). ThOD - 2.21 (based on calculation). BOD_{10} - 76% of ThOD BOD_{15} - 83% of ThOD BOD_{20} - 84% of ThOD
Test condition	COD Method = ASTM D1252-67 (reapproved 1974). BOD_5 Method = APHA Standard Methods No. 219,1971
Reference	Birdie, A.L., Wolff, C.J.M., and Winter, M. (1979). BOD and COD of some petrochemicals. Water Res. 13:627-630.
BOD_5/COD Ratio	no data
BOD_5	56% of ThOD
Concentrations	3, 7, 10 mg/L
Method	APHA Standard Methods 1989.
Reference	Waggy, G.T., Conway, R.A., Hansen, J.L., and Blessing, R.L. (1994). Comparison of 20-d BOD and OECD closed-bottle biodegradation tests. Environ. Toxicol. Chem. 13:1277-1280.

3.7 Bioaccumulation

Species	haddock (adult)
Temperature	7 °C
BCF	0.69

Year	1931
GLP	no
Test condition	static
Reference	Rustung, E., Koren, F., and Föyen, A. (1931). Über Aufnahme und von Aceton im Organismus von Kaltblütern. Biochem. Z. 242:366-376.

4. Ecotoxicity

4.1 Acute/Prolonged Toxicity to Fish

Type	flow through
Species	Salvelinus fontinalis
Exposure Period	96 h
LC_{50}	6070 mg/L
Analyt. Monitoring	no data
GLP	no data
Test Substance	no data
Remark	The exposure process is described in U.S. EPA: Methods for Acute Toxicity Tests with Fish, Macro-invertebrates, and Amphibians. EPA-660/3-75-009. Committee on Methods for Toxicity Tests with Aquatic Organisms (1975). The methods used by Cardwell et.al. (1974) are similar in duration of exposure, type of test vessel, physical/chemical parameters monitored, selection of dilution water, and selection of test species.
Reference	Cardwell, R.D., Foreman, D.G., Payne, T.R., and Wilber, D.J. (1974). Acute and chronic toxicity of four organic chemicals to fish. Project Report to C.E. Stephen, U.S. EPA, Environmental Research Laboratory - Duluth. Duluth, MN.

Type	flow through
Species	Lepomis macrochirus
Exposure Period	96 h
LC_{50}	7300 mg/L
Analyt. Monitoring	no data
GLP	no data
Test Substance	no data
Remark	Test Method similar to U.S. EPA: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians. EPA-660/3-75-009. Committee on Methods for Toxicity Tests with Aquatic Organisms, 1975.

Reference	Cardwell, R.D., Foreman, D.G., Payne, T.R., and Wilber, D.J. (1974). Acute and chronic toxicity of four organic chemicals to fish. Project Report to C.E. Stephen, U.S. EPA, Environmental Research Laboratory - Duluth. Duluth, MN.
Type	flow through
Species	Pimephales promelas
Exposure Period	96 h
LC_{50}	9100 mg/L
Analyt. Monitoring	no data
GLP	no data
Test Substance	no data
Remark	Test method similar to U.S. EPA: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians. EPA-660/3-75-009. Committee on Methods for Toxicity Test with Aquatic Organisms, 1975.
Reference	Cardwell, R.D., Foreman, D.G., Payne, T.R., and Wilber, D.J.(1974). Acute and chronic toxicity of four organic chemicals to fish. Project Report to C.E. Stephen, U.S. EPA - Environmental Research Laboratory - Duluth. Duluth, MN.
Type	static
Species	Gambusia affinis
Exposure Period	72 h
LC_{50}	13,000 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Results	24-h LC_{50} = 13,500 mg/L 48-h LC_{50} = 13,000 mg/L Below 11,500 mg/L, the fish showed no permanent distress.
Remark	Method similar to Doudoroff et al., Bioassay methods for the evaluation of acute toxicity of industrial wastes to fish. Sewage Ind. Wastes 23:1380-1397, 1951.
Reference	Wallen, I.E., Greer, W.C., and Lasater, R. (1957). Toxicity to Gambusia affinis of certain pure chemicals in turbid waters. Sewage Ind. Wastes 29:695-711.
Type	flow through
Species	Pimephales promelas

Exposure Period	96 h
LC_{50}	8120 mg/L
Analyt. Monitoring	yes
GLP	no data
Test Substance	no data
Remark	Method similar to: Methods for Measuring the Acute Toxicity of Effluents to Aquatic Organisms. W. Piltier, Bioassay Subcommittee. EPA Biological Advisory Committee, Ecology Branch. EPA-600/4-28-012, 1978.
Reference	Veith, G. (1983). Structure-toxicity relationships for the fathead minnow, Pimaphales promelas: Narcotic industrial chemicals. Can. J. Fish Aquat. Sci. 40:743-748.

Type	static
Species	Oncorhynchus mykiss
Exposure Period	96 h
LC_{50}	5540 mg/L
Analyt. Monitoring	no data
GLP	no data
Test Substance	prescribed by 1.1-1.4
Remark	Method similar to: Methods for Measuring the Acute Toxicity of Effluents to Aquatic Organisms. W. Piltier, Bioassay Subcommittee. EPA Biological Advisory Committee, Ecology Branch, EPA-600/4-28-012, 1978.
Reference	Johnson, W.W. and Finley, M.T. (1980). Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Department of the Interior Fish and Wildlife Service. Resource Publication 137. Washington, DC.

Type	flow through
Species	Pimephales promelas
Exposure Period	96 h
LC_{50}	6210-8120 mg/L
Analyt. Monitoring	yes
GLP	no data
Test substance	no data
Test method	similar to OECD Guideline 204.
Remark	Results from 3 test runs (LC_{50} in mg/L): 24-h: 8830, 9400, 8030 72-h: 8120, 7940, 6400 96-h: 8120, 7280, 6210
Reference	Brooke, L.T., Call, D.J., Geiger, D.L., and Northcott, C.E. (1984). Acute Toxicities of Organic Chemicals to Fathead

Minnows (Pimephales promelas). Center for Lake Superior Environmental Studies.

Type	static
Species	Poecilia reticulata
Exposure Period	14 day
LC_{50}	6400 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Test method	similar to U.S. EPA: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians. EPA-660/3-75-009. Committee on Methods for Toxicity Tests with Aquatic Organisms, 1975.
Reference	Konemann, H. (1981). Quantitative structure-activity relationships in fish toxicity studies. Part 1: Relationship for 50 industrial pollutants. Toxicology 9:209-221.

Type	flow through
Species	Salmo gairdneri
Exposure Period	24 h
LC_{50}	6100 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Acetone (2930 mg/L) produced an increase in ventilation rate, reaching a maximum of 158% of controls at 21 hours for the duration of the exposure period.
Remark	Method similar to that contained in: Sprague, J.B. (1969). Measurement of pollutant toxicity to fish. I. Bioassay methods for acute toxicity. Water Res. 3:793-821.
Reference	Majewski, H.S., Klaverkamp, J.F., and Scott, D.P. (1978). Acute lethality and sub-lethal effects of acetone, ethanol, and propylene glycol on the cardiovascular and respiratory systems of rainbow trout (Salmo gairdneri). Water Res. 13:217-221.

Type	static
Species	Lepomis macrochirus
Exposure Period	96 h
LC_{50}	8300 mg/L
Analyt. Monitoring	no data
GLP	no

Test substance	no data
Remark	Test method similar to Doudoroff, P. (1951). Bioassay methods for the evaluation of acute toxicity of industrial wastes to fish. Sewage Ind. Wastes 23:1380-1397.
Reference	Cairns, J. and Scheier, A. (1968). A comparison of the toxicity of some of the common industrial waste components tested individually and combined. Progressive Fish Culturist 30:3-8.

Type	static
Species	Carassius auratus
Exposure Period	24 h
LC_{50}	>5000 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Method similar to that described in: American Public Health Association. Review papers on measurement of pollutant toxicity to fish. Sprague, J.B. (1969). Bioassay methods for acute toxicity. Water Res. 3:793-821.
Reference	Birdie, A.L., Wolff, C.J.M., and Winter, M. (1979). The acute toxicity of some petrochemicals to goldfish. Water Res.13:623-626.

Type	static
Species	Leuciscus idus
Exposure Period	48 h
LC_{50}	7505-11,300 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Test method similar to: U.S. EPA: Methods for acute toxicity tests with fish, macroinvertebrates, and amphibians. EPA-660/3-75-009. Committee on methods for toxicity tests with aquatic organisms, 1975.
Reference	Juhuke, I. and Luedemann, D. (1978). Results of the study of 200 chemical compounds on acute toxicity using the golden orfe test. Z. Wasser Abwasser Forsch. 11:161-164.

Type	flow through
Species	Pimephales promelas
Exposure Period	1 h
LC_{50}	6210-8030 mg/L

Analyt. Monitoring	yes
GLP	no data
Test substance	no data
Remark	Test method similar to U.S. EPA: Methods for acute toxicity test with fish, macroinvertebrates, and amphibians. EPA-660/3-75-009. Committee on Methods for Toxicity Test with Aquatic Organisms, 1975.
Result	Results of 3 test runs are as follows (LC_{50} in mg/L): 24-h: 8830, 9400, 8030 48-h: 8290, 8880, 7940 72-h: 8120, 7940, 6400 96-h: 8120, 7280, 6210 Test substance minimum purity 90%; analysis of test article in water from fish exposure tanks.
Reference	Brooke, L.T., Call, D.J., Geiger, D.L., and Northcott, C.E. (1984). Acute toxicities of organic chemicals to fathead minnows (Pimephales promelas). Center for Lake Superior Environmental Studies. University of Wisconsin - Superior. pp. 319.

4.2 Acute Toxicity - Aquatic Invertebrates

Species	Daphnia magna
Exposure Period	48 h
LC_{50}	12,600 & 12,700 mg/L (two laboratories)
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Tests conducted according to a protocol from the Dutch Standard Institute (Adema, 1978).
Reference	Canton, J.H. and Adema, D.M.M. (1978). Repro-ducibility of short-term and reproduction toxicity experiments with Daphnia magna and comparison of the sensitivity of Daphnia magna with Daphnia pulex and Daphnia cucullata in short-term experiments. Hydrobiologia 59:135-140.

Species	Daphnia pulex
Exposure Period	48 h
LC_{50}	8800 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Tests conducted according to a protocol from the Dutch

	Standard Institute (Adema, 1978).
Reference	Canton, J.H. and Adema, D.M.M. (1978). Repro-ducibility of short-term and reproduction toxicity experiments with Daphnia magna and comparison of the sensitivity of Daphnia magna with Daphnia pulex and Daphnia cucullata in short-term experiments. Hydrobiologia 59:135-140.

Species	Daphnia cucullata
Exposure Period	48 h
LC_{50}	7635 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Tests conducted according to a protocol from the Dutch Standard Institute (Adema, 1978).
Reference	Canton, J.H. and Adema, D.M.M. (1978). Repro-ducibility of short-term and reproduction toxicity experiments with Daphnia magna and comparison of the sensitivity of Daphnia magna with Daphnia pulex and Daphnia cucullata in short-term experiments. Hydrobiologia 59:135-140.

Species	Daphnia magna
Exposure Period	48 h
LC_{50}	13,500 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Procedure used individuals 12-hours old. The test water was from a local spring-fed pond with an average hard-ness 154.5 mg/L, pH of 7.7, and temperature of 22°C.
Reference	Randall, T.L. and Knopp, P.V. (1980). Detoxification of specific organic substances by wet oxidation. J. Water Pollut. Control Fed. 52:2117-2130.

Species	Daphnia magna
Exposure Period	24 h
LC_{50}	>10,000 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Procedure used individuals 24-hours old. Test used tap water free of chlorine, saturated with oxygen, hardness 16 (German), pH 7.6-7.7, temperature 20-22°C.

Reference	Bringmann, V.G. and Kuhn, R. (1977). Results of the damaging effect of water pollutants on Daphnia magna. Z. Wasser Abwasser Forsch. 10:161-166.
Species	Daphnia pulex
Exposure Period	18 h
LC_{50}	1550 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Test containers selected for compatibility with the size of the test organism. Duplicate test chambers with 10-12 concentrations. Test duration was 18 hours of which 16 hours were fluorescent illumination. Water temperature 23°C plus or minus 2°C. No supplemental food or air.
Reference	Bowman, M.C., Oller, W.L., and Cairns, T. (1981). Stressed bioassay systems for rapid screening of pesticide residues. Part I: Evaluation of bioassay systems. Arch. Environ. Contam. Toxicol. 10:9-24.
Species	Culex restuans (white-dotted mosquito)
Exposure Period	18 h
LC_{50}	7840 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Test containers selected for compatibility with the size of the test organism. Duplicate test chambers with 10-12 concentrations. Test duration was 18 hours of which 16 hours were fluorescent illumination. Water temperature was 23°C plus or minus 2°C. No food or air added.
Reference	Bowman, M.C., Oller, W.L., and Cairns, T. (1981). Stressed bioassay systems for rapid screening of pesticide residues. Part I: Evaluation of bioassays systems. Arch. Environ. Contam. Toxicol. 10:9-24.
Species	Hyalella azteca
Exposure Period	18 h
LC_{50}	3520 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Test containers selected for compatibility with the size of

	the test organism. Duplicate test chambers with 10-12 concentrations. Test duration was 18 hours of which 16 hours were fluorescent illumination. Water temperature was 23°C plus or minus 2°C. No food or air added.
Reference	Bowman, M.C., Oller, W.L., and Cairns, T. (1981). Stressed bioassay systems for rapid screening of pesticide residues. Part I: Evaluation of bioassay systems. Arch. Environ. Contam. Toxicol. 10:9-24.

Species	Lithodes antarcticus (southern king crab, larval stage)
Exposure Period	120-192 h.
EC_{50}	1010-4660 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	as prescribed by 1.1-1.4
Test method	American Public Health Association for Static Bioassay Procedures (APHA, AWWA, WPCF) 1976.
Remark	The mortality curve of larvae exposed to 7500 mg/L acetone (acetone controls) did not differ from that of seawater controls.
Result	Results as LC_{50} in mg/L are as follows: 120-h: 4660 144-h: 3880 168-h: 2330 192-h: 1010
Reference	Lombardo, R.J., Ferrari, L., and Vinuesa, J.H. (1991). Effects of lindane and acetone on the development of larvae of the southern King Crab (Lithodes antarcticus). Bull. Environ. Contam. Toxicol. 46:185-192.

Species	Streptocephalus rubricaudatus
Exposure Period	24 h
LC_{50}	64,300 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	The hatching and 24-h toxicity test procedure used dry-stored cysts of S. rubricaudatus (originating from Algeria). Hatching was obtained by hydrating dried cysts in a petri dish in U.S. EPA freshwater medium (1985). After 18 hours incubation (at 25°C), the free-swimming larvae were pipet-transferred into a second petri dish for a supplemental period of 6 h. The test endpoint was death, defined by the

	complete lack of movement during 10 seconds of observation under a dissection microscope.
Reference	Crisinel, A., Delaunay, L., Rossel, D., and Tanadellas, J. (1994). Cyst-based ecotoxicological tests using Anostracans: comparison of two species of Streptocephalus. Environ. Toxicol. Water Qual. 9:317-326.

Species	Daphnia magna
Exposure Period	48 h
LC_{50}	104,712 µmol/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Age of test organism was less than 2 days; number of test organisms per group was 25; test volume was 1 L; temperature was 22°C plus or minus 1°C; hardness was approximately equal to one.
Reference	Hermens, J., Cantor, H., Janssen, P., and DeJong, R. (1984). Quantitative structure-activity relationships and toxicity studies of mixtures of chemicals with anesthetic potency: acute lethal and sublethal toxicity to Daphnia magna. Aquatic Toxicol. 5:143-154.

4.3 Toxicity to Aquatic Plants e.g. Algae

Species	Chlorella pyrenoidosa
Endpoint	see below
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Also tested was the green algae, Scenedesmus quadricauda. Photosynthesis was used as the test criterion and was quantified by monitoring the uptake of $^{14}CO_2$ from $NaH^{14}CO_3$, as previously described by Stratton et al. (1980). Acetone alone was not inhibitory to either S. quadricauda or C. pyrenoidosa. Photosynthetic activity in these species was stimulated above 0.2% acetone while stimulatory activity increased 30-40% at an acetone concentration of 1.0%.
Method	Method similar to: Stratton, G.W. et al. (1980). Bull. Environ. Contam. Toxicol. 24:562.
Reference	Stratton, G.W. and Corke, C.T. (1981). Interactions between acetone and two pesticides toward unicellular

green algae. Bull. Environ. Contam. Toxicol. 27:13-16.

Species	Chlorella pyrenoidosa
Endpoint	growth rate
Exposure Period	14 day
EC_{50}	3020 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Exposure Period	10-14 days.
Remark	Growth was monitored by following the increase in optical density over time for 10-14 days using a spectrophotometer equipped with a universal test tube adapter and appropriate filters. Effects of acetone were assayed against the growth of C. pyrenoidosa at five to ten concentrations ranging from 0.1% to 6.0%.
Reference	Stratton, W.S. and Smith, T.M. (1988). Interaction of organic solvents with the green alga Chlorella pyrenoidosa. Bull. Environ. Contam. Toxicol. 40:736-742.

Species	Chlorella pyrenoidosa
Endpoint	Effects on membrane integrity and cell leakage
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Acetone-induced leakage from C. pyrenoidosa was monitored by following the loss of carbon compounds from cells using radioisotopic techniques. The cells were radiolabeled photosynthetically using ^{14}C-sodium bicarbonate. Significant leakage occurred at 1.5% and lower (depending on the exposure period (i.e., 24, 48, or 96 h).
Reference	Stratton, G.W. (1989). Effect of the solvent acetone on membrane integrity in the green alga, Chlorella pyrenoidosa. Bull. Environ. Contam. Toxicol. 42:754-760.

Species	Anabaena inaequalis
Endpoint	photosynthetic ability
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Method	Cells were incubated for 2 h and harvested by filtration through 0.45 μm membrane filters. Photosynthetic changes

	were noted by monitoring the uptake of $^{14}CO_2$ from $NaH^{14}CO_3$. The amount of radioactivity incorpor-ated into the cells was determined using a liquid scintillation counter. Percent inhibition was calculated. Anabaena cylindrica and Anabaena variabilis also examined.
Remark	A. inaequalis photosynthetic activity was significantly altered at acetone concentrations of 1000 mg/L and 4000 mg/L, where stimulation was observed. A. variabilis photosynthesis was significantly stimulated by acetone concentrations below 10,000 mg/L. No significant stimulation of $^{14}CO_2$ uptake occurred with A. cylindrica, although inhibition was observed above 6000 mg/L acetone. Inhibition was 75% at 8000 mg/L and 95% at 10,000 mg/L.
Reference	Stratton, G.W., Burrell, R.E., Krup, M.L., and Corke, C.T. (1980). Interactions between the solvent acetone and pyrethroid insecticide permethrin on activities of the blue-green alga Anabaena. Bull. Environ. Contam. Toxicol. 24:562-569.

Species	Anabaena inaequalis
Endpoint	nitrogen fixation ability
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Method	Assayed using the acetylene reduction technique. After the addition of a 10% atmosphere of acetylene, the cells were incubated for 5 h and the ethylene produced was assayed by gas chromatography. A. variabilis was not included in these studies due to its inability to fix nitrogen. Anabaena cylindrica and Anabaena variabilis were also examined
Remark	A. inaequalis activity was stimulated by all acetone concentrations from 1000 mg/L to 10,000 mg/L. The degree of stimulation was greater than that observed in photosynthetic studies. A. cylindrica exhibited significantly increased acetylene reduction at levels of acetone less than 4000 mg/L and decreased significantly at levels greater than 5000 mg/L.
Reference	Stratton, G.W., Burrell, R.E., Krup, M.L., and Corke, C.T. (1980). Interactions between the solvent acetone and pyrethroid insecticide permethrin on activities of the blue-green alga Anabaena. Bull. Environ. Contam. Toxicol. 24:562-569.

Species	Skeletonema costatum
Endpoint	growth sensitivity
Analyt. Monitoring	no data
Year	1988
GLP	no data
Test substance	no data
Remark	S. costatum was cultured in growth medium to achieve the selected density of 100,000 cells/mL. Total cell count and total cell volume were measured by use of a Coulter counter.
Result	Classified as practically nontoxic (> 100 mg/L).
Reference	Cowgill, U.M., Milazzo, D.P., and Landenberger, B.D. (1989). Toxicity of nine benchmark chemicals to Skeletonema costatum, a marine diatom. Environ. Toxicol. Chem. 8:451-455.

Species	Scenedesmus quadricauda
Endpoint	toxicity threshold
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Additional Species tested was Microcystis aeruginosa. Test cultures prepared from the dilution series and the control cultures were kept under standardized conditions for 8 days with constant lighting at 27 °C. Cultures were shaken daily and the concentration of the algal suspen-sions of each test culture was measured turbidimetrically.
Result	The chemical concentration causing the onset of cell multiplication inhibition was defined as the toxicity threshold. The toxicity threshold was 7500 mg/L for S. quadricauda and 530 mg/L for M. aeruginosa.
Reference	Bringmann, G. and Kuhn, R. (1978). Testing of substances for their toxicity threshold: model organisms Microcystis (Diplocystis) aeruginosa and Scenedesmus quadricauda. Mitt. Internat. Verein. Limnol. 21:275-284.

4.4 Toxicity to Bacteria

Type	aquatic
Species	Paramaecium caudatum
Exposure Period	4 h
LC_{50}	6800 mg/L

Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Method described in: Stressed bioassay systems for rapid screening of pesticide residues. I. Evaluation of bioassay systems. Environ. Contam. Toxicol. 10:9-24. (1981).
Reference	Rajini, P.S., Krishnakumare, M.K., and Majunder, S.K. (1989). Cytotoxicity of certain organic solvents and organophosphorus insecticides to the ciliated protozoan Paramecium caudatum. Microbios 59:157-163.

Type	other
Species	Uronema parduzci
Endpoint	toxicity threshold
Exposure Period	20 h
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	The protozoan test Species was fed with pure inactive cultures of E. coli to avoid metabolism of the test article by the bacteria. The test period for determination of a toxicity threshold was 20 h. Quantification of bacteria (food) and protozoa (test species) was done by cell counter. A 5% difference in protozoan cell count between test article and control was used to determine the toxicity threshold.
Result	Result is given as a toxicity threshold of 1710 mg/L.
Reference	Bringmann, G. and Kuhn, R. (1980). Determination of the harmful effect of water pollutants on protozoa. II. Bacteriovorous ciliates. Z. Wasser Abwasser Forsch. 13:26-31.

Type	other
Species	Chilomonas paramecium
Endpoint	toxicity threshold
Exposure Period	48 h
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	The flagellate saprozoic protozoan test species was fed pure inactive cultures of E. coli to avoid metabolism of the test article by the bacteria. The test period for determination of a toxicity threshold was 48 h. Quantification of bacteria(food) and protozoa (test species)

	was by electronic cell counter. A 5% difference in protozoan cell count between test Species and controls was used to determine the toxicity threshold.
Result	Result is reported as a toxicity threshold of 3516 mg/L.
Reference	Bringmann, G. and Kuhn, R. (1980). Determination of biological damage from water pollutants to protozoa. III. Saprozoic flagellates. Z. Wasser Abwasser Forsch. 13:170-173.

Type	other
Species	Entosiphon sulcatum
Exposure Period	72 h
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	The protozoan test Species was fed pure inactive cultures of E. coli to avoid metabolism of the test article by the bacteria. The test period for determination of a toxicity threshold was 72 h. Quantification of bacteria (food) and flagellates (test species) was performed by electronic cell counter. A 5% difference in protozoan cell count between test species and controls was used to determine the toxicity threshold.
Result	Result is reported as a toxicity threshold of 28 mg/L.
Reference	Bringmann, G. and Kuhn, R. (1978). Determination of the biological toxicity of water-bound substances towards protozoa. I. Bacteriovorous flagellates (model organism: Entosiphon sulcatum). Z. Wasser Abwasser Forsch. 11:210-215.

Type	aquatic
Species	Pseudomonas putida
Endpoint	oxygen uptake
Analyt. Monitoring	no data
GLP	no data
Test substance	as prescribed by 1.1-1.4
Remark	Oxygen uptake was measured over a 10-min. period at 27°C before, during, and after sample addition. Growth was determined by inoculating P. putida into medical flats and incubating at 27°C. Thirty minutes before inoculation with acetone, the test cultures were diluted with fresh medium to a density with an absorption of approximately 0.8 at 600 µm measured spectrophotometrically. The test

	solutions were redistributed to medical flats, acetone added, and incubated for 6 hours at 27°C. Growth was terminated by formalin addition and immediately followed by density measurements.
Result	Oxygen uptake over 10 min (EC_{10}) was 1380 mg/L. Growth inhibition over 7 h (EC_{10}) was 540 mg/L.
Reference	Slabbert, J.L. and Grabow, W.O.K. (1986). A rapid water toxicity screening test based on oxygen uptake of Pseudomonas putida. Toxicity Assess. 1:13-26.

Type	aquatic
Species	Escherichia coli
Endpoint	minimal inhibitory concentrations (MIC)
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	Test Species was a mutant strain with enhanced sensitivity to a wide spectrum of toxic substances. The assay is based on the ability of toxicants to inhibit the de novo synthesis of an inducible enzyme, e.g., β-galactosidase, by a rough mutant of E. coli, which is highly sensitive to a wide spectrum of toxic substances.
Result	The minimal inhibitory concentration (MIC) was 25,000 mg/L (defined as the concentration causing 20% toxicity).
Reference	Reinhartz, A., Lampert, I., Herzberg, M., and Fish, F. (1987). A new short-term sensitive bacterial assay kit for the detection of toxicants. Toxicity Assess. 2:193-206.

Type	aquatic
Species	Polytox (proprietary blend of 12 aerobic bacteria strains)
Exposure Period	6 h
IC_{50}	48,000 mg/L
Analyt. Monitoring	no data
GLP	no data
Test substance	no data
Remark	The percent inhibition at different concentrations of acetone was based on the reduction in oxygen uptake rate of spiked reactors compared to that of the control reactor. Plotted against the respective concentrations, the concentration causing 50% inhibition or IC_{50} was determined.
Reference	Nirmalakhandan, N., Arulgnanendran, V., Mohsin, M., Sun, B., and Cadena, F. (1994). Toxicity of mixtures or

organic chemicals to microorganisms. Water Res. 28:543-551.

Type	aquatic
Species	activated sludge of a predominantly domestic sewageEC_{50}77.4 mg/L
Analyt. Monitoring	no data
Method	ISO 8192
Year	1991
GLP	no data
Test substance	as prescribed by 1.1-1.4
Remark	Activated sludge of a predominantly industrial sewage was also tested.
Result	EC_{50} for the industrial/synthetic sewage was 59.4 mg/L.
Reference	Kilroy, A.C. and Gray, N.F. (1992). The toxicity of four organic solvents commonly used in the pharmaceutical industry to activated sludge. Water Res. 26:887-892.

Type	aquatic
Species	activated sludge
Exposure Period	16 h
EC_{50}	>5000 mg/L
Analyt. Monitoring	no data
Method	OECD Guideline 209
GLP	no data
Test substance	no data
Reference	Alsop, G.M., Waggy, G.T., and Conway, R.A. (1980). Bacterial growth inhibition test. J. Water Pollut. Control Fed. 52:2452-2456.

Type	aquatic
Species	activated sludge of a predominantly domestic sewage
Exposure Period	3 h
EC_{50}	>1000
Analyt. Monitoring	no data
Method	OECD Guideline 209
GLP	no data
Test substance	as prescribed by 1.1-1.4
Reference	Klecka, G.M. and Landi, L.P. (1985). Evaluation of the OECD activated sludge respiration inhibition test. Chemosphere 14:1239-1251.

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species	Lithodes antarcticus
Endpoint	mortality
Exposure	7 day
EC_{50}	>0.75 g/L
Analyt. Monitoring	no data
GLP	no data
Test substance	as prescribed by 1.1-1.4
Method	The experiments were conducted following the recommendations of the APHA, AWWA, WPCF Standard Methods for the examination of water and wastewater, 14th ed., Am. Pub. Health Assoc., Washington, D.C. 1976, i.e. 7-day, 48-h static renewal. 8°C and 35 parts per thousand salinity.
Remark	Mortality in the seawater controls was lower than 10% during the first seven days of culture and the acetone controls (0.75 g/L) did not show mortality above that of the seawater controls during this period.
Reference	Lombardo, R.J., Ferrari, L., and Vinuesa, J.H. (1991). Effects of lindane and acetone on the development of larvae of the Southern King Crab (Lithodes antarcticus Jaquinot). Bull. Environ. Contam. Toxicol. 46:185-192.

4.6 Toxicity to Terrestrial Organisms

4.6.2 Toxicity to Terrestrial Plants

Species	Raphanus sativus L. var. Champion 708 (radish)
Endpoint	emergence and growth
Exposure Period	7 day
NOEC	100 mg/L
GLP	no
Test substance	no data
Remark	Also tested were Lactuca sativa L. var. 525 Ithaca M.T.O. (lettuce) and Lolium perenne L. var. Manhattan (rye grass).
Method	The bioassay was most similar to the blotter-sandwich technique, and was designed to determine the dose-response characteristics of acetone on the germination and early growth of three representative terrestrial plants during a 7-day exposure period.
Result	7-day NOEC for all three Species was 100 mg/L.
Reference	Gorsuch, J.W., Kringle, R.O., and Robillard, K.A. Chemical effects on the germination and early growth of

terrestrial plants (1990). In: Plants for Toxicity Assessment, ASTM STP 1091. W. Wang, J.W. Gorsuch, and W.R. Lower, eds., pp. 49-58. American Society for Testing and Materials. Philadelphia, PA.

Species	Zea mays L. var. rugosa Bouaf
Endpoint	Total germination and percentage of normal seedlings
Exposure Period	5 sec., 0.25, 0.50, 1.0, 2.0, 4.0, or 8.0 h; immersion in 100% acetone.
GLP	no data
Test substance	as prescribed by 1.1-1.4
Method	The organic solvent infusion technique has been used successfully to improve germination.
Remark	Total germination and percentage of normal seedlings in both cultivars (Florida Staysweet and Crisp-n-Sweet 710) were significantly decreased after 8 h of immersion in acetone. Average seedling dry weight, however, did not decrease. Results indicate that acetone could be used as an infusion agent for fungicides in the seed of some sweet corn cultivars without compromising seed germination or vigor.
Reference	Hung, P.E. (1992). Infusion of shrunken-2 sweet corn seed with organic solvents: effects on germination and vigor. Horticult. Sci. 27:467-470.

Species	Cucumis sativus (long green cucumber)
Endpoint	active dormancy - breaking factor
Exposure Period	various
Year	1993
GLP	no data
Test substance	as prescribed by 1.1-1.4
Method	Dormant and non-dormant seeds were immersed in acetone in glass-stoppered containers at 10°C for various time periods. After treatment the seeds were allowed to air-dry for 24 h in open petri dishes and then used in germination experiments.
Remark	Acetone was found not only to break the dormancy in cucumber seeds, but also to prevent its induction by far-red light. The data also show that prevention of dorm-ancy development as well as breakage of dormancy by acetone are accompanied by a change in the permeability of the cell membrane of the perisperm-endosperm envelope around the embryo.

Reference	Amritphale, D., Dixit, S., and Singh, B. (1993). Effect of acetone on the induction and breakage of secondary dormancy in seeds of cucumber. J. Exp. Botany. 44:1621-1626.

4.6.3 Toxicity Non-Mammalian Terrestrial Species

Species	Coturnix coturnix japonica
Endpoint	mortality
Exposure Period	5 days
LC_{50}	>20,000 ppm
GLP	no data
Test substance	as prescribed by 1.1-1.4
Method	5-day dietary trial with 14-day old coturnix quail.
Remark	Total mortality was 0/45 at 5 days.
Reference	Hill, E. F. and Carmardese, M.B. (1986). Lethal dietary toxicities of environmental contaminants and pesticides to Coturnix. Patuxent Wildlife Research Center. Laurel, MD. pp. 22-23.

4.7 Biological Effects Monitoring

Remark	The bioaccumulation potential of a chemical in muscle tissue from rainbow trout has been shown to be related to the octanol water partition coefficient. The partition coefficient for acetone of -0.24 indicates a high degree of water solubility and low potential to bioaccumulate or biomagnify in the environment.
Reference	Paterson, S. and Mackay, D. (1989). Correlation of tissue, blood and air partition coefficients of volatile organic chemicals. Br. J. Ind. Med. 46:321-328. Neely, W.B., Branson, D.R., and Blau, G.E. (1974). Partition coefficient to measure bioconcentration potential of organic chemicals in fish. Environ. Sci. Technol. 8:1113-1115.

4.8 Biotransformation and Kinetics

Type	plant
Remark	The objective of the experiment was to determine if acetone inhibits the mutagenic activity of promutagenic dimethylnitrosamine (DMN) and methylbutylnitrosamine

in a higher plant, Arabidopsis thaliana. Seeds were immersed for 3 hours at 25°C in 1 mL of acetone mixed with buffer for pretreatment. They were then immersed for 3 hours at 25°C in 2 mL of the mixture containing the mutagens and acetone for treatment. Following treatment, the seeds were rinsed for 30 min in distilled water and sown on soil in a greenhouse.

Result The frequency of mutations and the degree of sterility induced by DMN was markedly reduced in the presence of acetone.

Reference Gichner, T. and Veleminsky, J. (1986). Organic solvents inhibit the mutagenicity of promutagens dimethyl-nitrosamine and methylbutylnitrosamine in a higher plant Arabidopsis thaliana. Mutagenesis 1:107-109.

Type animal (Daphnia magna)

Remark The hypothesis of constancy of the tissue residues in animals treated with narcotic organic chemicals was tested by determining the effect of body length, time, and ambient concentration on tissue concentration in Daphnia magna narcotized by exposure to toxic levels of acetone.

Result The lower than expected toxicity of acetone may be due to the degradation of this chemical by Daphnia. Acetone, a simple organic compound, may be readily metabolized by Daphnia. As a result, some of the radioactivity in Daphnia tissues would be associated with accumulated metabolites rather than the original compound, and the narcotizing body burdens of acetone would be over-estimated. Acetone did not exert a significant negative influence on the effective internal concentration. When predicted body burdens for acetone were calculated using mean body sizes, exposure concentrations, and exposure durations, body burden acetone residues of 115 mmole/kg were more than an order of magnitude from the overall mean for all narcotics tested.

Reference Pawlisz, A.V. and Peters, R.H. (1993). A test of the equipotency of internal burdens of nine narcotic chemicals using Daphnia magna. Environ. Sci. Technol. 27:2801-2806.

Type other

Remark This paper reports the results of a research program concerned with the analyses and explanation of differences in sensitivity of species to toxic substances using biological properties of the species. The project aims at the

development of predictive models, which, in analogy to QSARs, are called Quantitative Species Sensitivity Relationships. The distributions of acute toxicity data of different Species were studied for 26 chemicals.

Result Chemicals with a specific mode of action have large sensitivity ratios whereas inert chemicals with lower toxicity have lower ratios. Acetone had the lowest ratio of all twenty-six chemicals studies.

Reference Hoekstra, J.A., Vaal, M.A., Notenboom, J., and Sloof, W. (1994). Variations in the sensitivity of aquatic species to toxicants. Bull. Environ. Contam. Toxicol. 53:98-105.

Type plant (various species)

Remark This paper describes experiments conducted to test the effects of volatiles including (acetone) on seed deterioration during seed storage. Seeds tested were lettuce, soybean, sunflower, carrot, and rice. It has been shown that the yields of volatiles such as acetone in soybean seeds increase during seed development and decrease to trace levels after reaching yellow maturation. The authors showed in a preliminary study that the evolution of volatiles, such as acetone, is a widespread phenomenon occurring in stored seeds. Many types of dry seeds that were tested continued to evolve volatiles and accumulate them during storage. Acetone was found to have only slight deleterious effects on some species.

Reference Zhang, M., Maeda, Y., Furihata, Y., Nakamaru, Y., and Esashi, Y. (1994). A mechanism of seed deterioration in relation to the volatile compounds evolved by dry seeds themselves. Seed Sci. Res. 4:49-56.

Type aquatic (Daphnia magna)

Remark This work examines the hypothesis that exposure of Daphnia magna to sublethal levels of narcotic contaminants including acetone may affect subsequent sensitivity of animals. Prior exposure (24 h) of Daphnia to sublethal levels of acetone had no effect on their sensitivity to effective levels of these chemicals. Effective burdens (24-h acute exposure) were independent of the sublethal body burdens (24-h sublethal exposure) and of the sublethal water concentrations ($p < 0.025$). These results imply that animals from polluted sites should be no more resistant to high body residues of pollutants than those from clean sites

	and that the toxicity of narcotic organic compounds like acetone may be independent of the time course of uptake.
Reference	Pawlisz, A.V. and Peters, R.H. (1995). Effects of sublethal exposure on lethal body burdens of narcotic organic chemicals in Daphnia magna. Environ. Sci. Technol. 29:613-621.

4.9 Additional Reports

Remark	The objective of this paper is to compare the usefulness of a representative of the Urodela (Ambystoma mexicanum) and Anura (Xenopus laevis) species as biological indicators in toxicological bioassays. Toxicity test conditions were as follows: static, 1-L size, 20°C plus or minus 1°C, circadian light and dark schedule, 48-h exposure for acetone. The 48-h LC_{50} for A. mexicanum was 20,000 mg/L and the over 48-h LC_{50} for A. laevis was 24,000 mg/L.
Reference	Sloaff, W. and Baesselman, R. (1980). Comparison of the usefulness of Mexican Axolotl (Ambystoma mexicanum) and the clawed toad (Xenopus laevis) in toxicological bioassays. Bull. Environ. Contam. Toxicol. 24:439-443.
Remark	The effects of acetone on the growth of four fungi were determined to be as follows: EC_{50} for Polyporous hirsutus was greater than 2.0%, Pestalotia sp. was 1.25%, Sclerotinia homeocarpa was 0.88%, and Fusarium oxysporum was 1.8%. It was concluded that acetone was a moderately fungitoxic compound, but the specific mode of action was not elucidated.
Reference	Burrell, R.E. and Corke, C.T. (1980). Interactions of the solvent acetone with the fungicides benomyl and captan in fungal assays. Bull. Environ. Contam. Toxicol. 25:554-561.
Remark	This paper provides the 96-h TL_m (50% survival) for Lepomis macrochirus (bluegill sunfish) of 8300 ppm and the 120-h TL_m (50% reduction in number of cells produced) for the diatom Nitzschia linearis (widely distributed in unpolluted soft fresh waters of the U.S.) of 11,493-11,727 ppm acetone.
Reference	Patrick, R., Cairns, J., and Scheir, A. (1968). The relative sensitivity of diatoms, snails, and fish to twenty common

constituents of industrial wastes. Progressive Fish Culturist 30:137-140.

Remark

Acetone is often used as a carrier solvent in aquatic bioassays at 100 ppm without affecting the evaluation of the test article. This paper provides comparative chronic data for Daphnia magna and Pimephales promelas. Endpoints evaluated include: survival of adults, number of young per adult, primiparous instar, days to primiparous instar, and total number of broods for the daphnid. Fish endpoints included: embryo survival, hatching rate, larval survival, length and weight. Differences between the solvent control (acetone and dilution water) and control dilution water were minimal.

Reference

McCarthy, J.F. and Whitmore, D.K. (1985). Chronic toxicity of di-n-butyl and di-n-octyl phthalate to Daphnia magna and the fathead minnow. Environ. Toxicol. Chem. 4:167-179.

Remark

Static acute and flow-through toxicity tests were performed with Daphnia magna. The 48-h LC_{50} value for acetone was 39,000 µL/L. The maximum acceptable toxicant concentrations determined during the chronic toxicity test with acetone were between 1400 and 2800 µL/L. Acetone was sufficiently low in toxicity to suggest that the recommended usage limits for acetone as a co-solvent (500 µL/L during acute toxicity tests; 100 µL/L during chronic toxicity tests).

Reference

LeBlanc, G.A. and Surprenant, D.C. (1983). The acute and chronic toxicity of acetone, dimethylformamide, and triethylene glycol to Daphnia magna (Straus). Arch. Environ. Contam. Toxicol. 12:305-310.

Remark

A multi-species test procedure was used to measure the acute aquatic effects of acetone on seven aquatic species simultaneously: Asellus intermedius (pillbug), Daphnia magna (water flea), Dugesia tigrina (flatworm), Gammarus fasciatus (sideswimmer), Helisoma trivolvis (snail), Lumbriculus variegatus (segmented worm) and Pimephales promelas (fathead minnow). These species were chosen because of their ecological importance diversity, and amenability to laboratory culturing. The 96-h static LC_{50} for all species was > 100 mg/L.

Reference	Ewell, W.S., Gorsuch, J.W., Kringle, R.O., Robillard, K.A., and Spiegel, R.C. (1986). Simultaneous evolution of the acute effects of chemicals on seven aquatic species. Environ. Toxicol. Chem. 5:831-840.
Remark	The test species was Xenopus laevis and the endpoint was the minimum concentration inhibiting growth. The method was the frog embryo teratogenesis assay Xenopus (FETAX), as described by Damont et al. (1983). The 96-h bioassay determines the relative teratogenic potential. The purpose of this experiment was to determine whether carrier solvents interacted with the teratogens t-retinoic acid and 6-aminonicotinamide to affect survival, development, and growth of Xenopus embryos.
Result	The 96-h minimum concentrations that inhibited growth were: 18,000 mg/L for trial 1, 15,000 mg/L for trial 2, and 10,000 mg/L for trial 3.
Reference	Rayburn, J.R. Fort, D.J., McNew, R., and Bantel, J.A. (1991). Synergism and antagonism induced by three carrier solvents with t-retinoic acid and 6-aminonico-tinamide using FETAX. Bull Environ. Contam. Toxicol. 46:625-632.
Remark	The test species was Xenopus laevis and the endpoint was the reproduction rate for 12 weeks post-hatch at 0.10% acetone. The method uses groups of eggs that were put either in 800-mL jars or 3-L glass containers and maintained in aerated tap water at 22°C (plus or minus 1°C) under 16-h photoperiod conditions. According to the volume of water the eggs were reared in groups of 10 or 25. After hatching, tadpoles were fed Infusyl tablets. Each jar or tank was covered with a glass plate in order to limit evaporation. Water was changed weekly. Daily monitoring of egg and tadpole mortality was conducted throughout the first week of treatment. The metamorphosis pattern was investigated on surviving tadpoles.
Result	Growth by weight and development were slightly delayed in animals at the beginning of treatment (premetamor-phosis). After metamorphosis, the weight of juvenile Xenopus was higher than that of the water controls. It was speculated that acetone might first delay develop-ment; then because of feeding habits or other reasons, tadpoles could regain normal weight gain and even show a tendency

	for increased growth.
Reference	Marchal-Segault, D. and Tamade, F. (1981). The effects of lindane, an insecticide, on hatching and postembryonic development of Xenopus laevis (Daudin) Anauran Amphibian. Environ. Res. 24:250-258.

5. Toxicity

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type	LD_{50}
Species	rat
Value	ca. 5800 mg/kg
GLP	no data
Test substance	no data
Reference	Freeman, J.J. and Hayes, E.P. (1985). Acetone potentiation of acute acetonitrile toxicity in rats. J. Toxicol. Environ. Health 15:609-621.

Type	LD_{50}
Species	rat
Value	ca. 8400 mg/kg
GLP	no
Test substance	no data
Reference	Smyth, H.F., Carpenter, C.P., Weil, C.S., Pozzani, U.C., and Striegel, J.A. (1962). Range-finding toxicity data: List VI. Am. Ind. Hyg. Assoc. J. 23:95-107.

Type	LD_{50}
Species	rat
GLP	no
Test Substance	analytical grade acetone (ACS specifications).
Remark	Groups of 6-12 male and female Sprague-Dawley rats of various ages were intubated with neat acetone. They were observed for 1 week. LD_{50} values in g/kg (95% confidence limits) were: newborn, 1.7 (1.3-3.0), 14-day-old, 4.4 (3.1-6.3), young adults [80-160 g], 7.2 (5.4-9.5), older adults [300-470 g], 6.7 (6.1-7.3).
Reference	Kimura, E.T., Ebert, D.M., and Dodge, P.W. (1971). Acute toxicity and limits of solvent residue for sixteen organic solvents. Toxicol. Appl. Pharmacol. 19:699-704.

Type	LD_{50}
Species	mouse
Value	ca. 5250 mg/kg
GLP	no data
Test substance	no data
Remark	Male ddY mice weighing 24-27 g were intubated with acetone following ip injection of 0.16 mL of olive oil/g. LD_{50} value of 5250 mg/kg was reported with a 95% confidence range of 3580-7700 mg/kg.
Reference	Tanii, H., Tsuji, H., and Hashimoto, K. (1986). Structure-toxicity relationship of monoketones. Toxicol. Lett. 30:13-17.

5.1.2 Acute Inhalation Toxicity

Type	LC_0
Species	rat
Exposure Time	30 minute
Value 16,000 ppm	
GLP	no
Test substance	no data
Remark	Female rats were exposed (whole body exposure) to acetone at nominal air concentrations of the following: 6/6 rats died at 32,000 ppm; 1/6 animals exposed to 16,000 ppm acetone for 4 hours also died.
Reference	Smyth, H.F., Carpenter, C.P., Weil, C.S., Pozzani, U.C., and Striegel J.A. (1962). Range-finding toxicity data: List VI. Am. Ind. Hyg. Assoc. J. 23:95-107.

Type	LC_{50}
Species	rat
GLP	no
Test substance	no data
Remark	LC_{50} values with 95% confidence intervals for 4-hr and 8-hr exposures were 32,000 ppm (27,400-37,200) and 21,000 ppm (17,900-24,800). Exposure was to female Carworth Farms-Nelson rats.
Reference	Pozzani, U.C., Weil, C.S., and Carpenter, C.P. (1959). The toxicological basis of threshold limit values: 5. The experimental inhalation of vapor mixtures by rats, with notes upon the relationship between single dose inhalation and single dose oral data. Am. Ind. Hyg. Assoc. J. 20:364-

369.

5.1.3 Acute Dermal Toxicity

Type	LD_0
Species	rabbit
Value	>7400 mg/kg
GLP	no
Test substance	no data
Remark	Exposure time was 24 hours. Both sexes were used; skin was abraded. Test substance was "practical" grade.
Reference	Roudabush, R.L., Terhaar, C.J., Fassett, D.W., and Dziuba, S.P. (1965). Comparative acute effects of some chemicals on the skin of rabbits and guinea pigs. Toxicol. Appl. Pharmacol. 7:559-565.

Type	LD_0
Species	guinea pig
Value	> 7400 mg/kg
Method	other
GLP	no
Test substance	no data
Remark	Male Hartley-derived guinea pigs were used; abraded and intact skin was exposed for 24 h to a "practical" grade of acetone.
Reference	Roudabush, R.L., Terhaar, C.J., Fassett, D.W., and Dziuba, S.P. (1965). Comparative acute effects of some chemicals on the skin of rabbits and guinea pigs. Toxicol. Appl. Pharmacol. 7:559-565.

Type	LD_{50}
Species	rabbit
Value	>15,700 mg/kg
GLP	no
Test substance	no data
Remark	Exposure was for a 24-h period. The hair was completely clipped from the trunk of four male albino rabbits. The dose was injected under an impervious plastic film (method of Draize et al., J. Pharmacol. Exp. Therap. 82:377, 1944). Animals were observed for 14 days.
Reference	Smyth, H.F., Carpenter, C.P., Weil, C.S. (1962). Range-finding toxicity data: List VI. Am. Ind. Hyg. Assoc. J. 23:95-107.

5.2. Corrosiveness and Irritation

5.2.1 Skin Irritation

Species	rabbit
Result	not irritating
Classification	not irritating
GLP	no
Test substance	no data
Remark	Exposure time was 24 h. Acetone, 0.01 mL, was applied to the shaved stomach of 5 rabbits.
Reference	Smyth, H.F., Carpenter, C.P., and Weil, C.S. (1962). Range-finding toxicity data: List VI. Am. Ind. Hyg. Assoc. J. 23:95-107.

5.2.2 Eye Irritation

Species	rabbit
Result	highly irritating
Classification	irritating
GLP	no
Test substance	no data
Method	20 µL of acetone was added to the center of cornea and the eye was read 18-24 h later and scored after staining with fluorescein.
Results	The dose administered was 15.8 mg. Acetone was assigned a rating of Grade 5 in system with maximum of Grade 10. The 10-grade ordinal series is based upon the degree of corneal necrosis that results from instillation of various volumes and concentrations of a chemical. Grade 1 indicates at most a very small area of necrosis resulting from 0.5 mL of undiluted chemical in the eye. Grade 5 indicates a severe burn from 0.005 mL, and grade 10 indicates a severe burn from 0.5 mL of a 1% solution in water or propylene glycol.
Reference	Carpenter, C.P. and Smyth, H.F. (1946). Chemical burns of the rabbit cornea. Am. J. Ophthamol. 29:1363-1372. Smyth, H.F., Carpenter, C.P., and Weil, C.S. (1962). Range-finding toxicity data: List VI. Am. Ind. Hyg. Assoc. J. 23:95-107.

Species	rabbit
Result	highly irritating
Classification	irritating
Method	Draize Test
GLP	no data
Test substance	no data
Remark	0.1 mL of acetone was placed in the conjunctival sac and the eye was scored at 24 h. The data from this study indicate that corneal thickening is directly related to eye irritation and damage (r=0.86). Acetone eye swelling (215%) was rated as severe. Irritancy ratings for aqueous solutions were: 3, 10, and 30% acetone, mild irritation; 1% acetone, mild/slight irritation; corneal thickening ratings for 1, 3, 10, and 30% aqueous acetone solutions were all mild.
Reference	Kennah, H.E.. Hignet, S., Laux, P.E., Dorko, J.D., and Barrow, C.S. (1989). An objective procedure for quantifying eye irritation based upon changes of corneal thickness. Fund. Appl. Toxicol. 12:258-268.

5.3 Sensitization

Type	Mouse ear swelling test
Species	mouse
Result	not sensitizing
Classification	not sensitizing
GLP	no data
Test substance	no data
Method	Following removal of hair with clippers, mice are injected twice intradermally in the test area with Freund's complete adjuvant. The mice are tape stripped in the application area, and the chemical or solution (0.1 mL) is applied topically. Stripping and application of the Test substance is repeated on three additional consecutive days. Seven days later, 20 µL of test compound or solution is applied to the left ear and 20 µL of the vehicle (if any) is applied to the right ear. Twenty-four and 48-h later, the ear thicknesses are measured while the animals are under light ether anesthesia.
Remark	This test was reported to have correctly identified 48/49 known human sensitizers and 23/23 known human nonsensitizers. The missed compound was a weak human sensitizer. Acetone was also not a sensitizer in a modified

	MEST that used a patch-test procedure for the sensitization step.
Result	Acetone was not a sensitizer in a similar mouse ear sensitization test (Descotes, 1988) or in a modification of the guinea pig maximization test of Magnusson and Kligman (Nakamura et al., 1994).
Reference	Gad, S.C., Dunn, B.J., Dobbs, D.W., Reilly, C., and Walsh, R.D.(1986). Development and validation of an alternative dermal sensitization test: The mouse ear swelling test (MEST). Toxicol. Appl. Toxicol. 84:93-114. Descotes, J. (1988). Identification of contact allergens: The mouse ear sensitization assay. J. Toxicol. Cutaneous Ocular Toxicol. 7:262-272. Nakamura, A., Momma, J., Sekiguchi, H., Noda, T., Yamano, T., Kaniwa, M., Kojima, S., Tsuda, M., and Kurokawa, Y. (1994). A new protocol and criteria for quantitative determination of sensitization potencies of chemicals by guinea pig maximization test. Contact Dermatitis 31:72-85.

5.4 Repeated Dose Toxicity

Species	mouse
Strain	B6C3F1
Sex	male/female
Route of Administration	drinking water
Exposure Period	14 days and 13 weeks
Frequency of Treatment	ad libitum
Post Exposure Observation Period	none
Doses	14 days: 0.5, 1.0, 2.0, 5.0, and 10.0%; 5 mice/sex. 13-week females: 0.25, 0.5, 1.0, 2.0, and 5.0%; 10 13-week males: 0.125, 0.25, 0.5, 1.0, and 2.0%; 10
Control Group	Yes
Method	OECD Guideline 407 OECD Guideline 408 was used for the 13-week studies.
GLP	yes
Test substance	as prescribed by 1.1-1.4
Remark	NOEL: 1% (males: 14 days, 1579 mg/kg; 13 weeks, 2258 mg/kg; females: 14 days, 3023 mg/kg; 13 weeks, 4156 mg/kg.

Remark	LOEL: 2% (males: 14 days, 3896 mg/kg; 13 weeks,
Remark	Mice, 6-7 weeks old at start of the study, were housed individually. Drinking water containing acetone and NIH 07 feed were provided ad libitum. The time-weighted average dosages were: 14-day males, 965, 1579, 3896, 6348, 10,314 mg/kg; 14-day females, 1569, 3023, 5481, 8804, 12,725 mg/kg; 13-week males, 380, 611, 1353, 2258, 4858 mg/kg; 13-week females, 892, 2007, 4156, 5945, 11,298 mg/kg. Body weights were determined weekly and water consumption twice weekly. At necropsy, liver, right kidney, right testis, heart, thymus, brain, lungs, and, at 13 weeks only, spleen were taken for determination of weights and histopathology. Blood samples were obtained before the 13-week sacrifice for measurement of hematological indices. Male reproductive endpoints were assessed and stage and length of the estrous cycle were evaluated in females.
Result	Water consumption, and thus acetone dose, was reduced at acetone concentrations of 5% and above. There were no deaths during the studies. Body weight gain was depressed in mice given 10% acetone in the 14-day study only. There were no treatment-related clinical signs of toxicity. Absolute and relative liver weights in female mice only were significantly elevated in the 13-week 5% group; similar increases were seen in the 14-day animals. Hematological changes observed in the 13-week animals were increased hematocrit in 5% females ($p < 0.01$), increased hemoglobin in 2% ($p < 0.05$) and 5% ($p < 0.01$) females and 0.5, 1.0, and 2% males ($p < 0.05$). Histopathological alterations were seen only in mice during the 14-day studies; these included centrilobular hepatocellular hypertrophy in 5 of 5 male mice in each of the 2, 5, and 10% groups, 2 of 5 females in the 5% group, and 5 of 5 females in the 10% group. There were no changes in male or female reproductive indices.
Reference	Dietz, D.D., Leininger, J.R., Rauckman, E.J., Thompson, M.B., Chapin, R.E., Morrissey, R.L., and Levine, B.S. (1991). Toxicity studies of acetone administered in the drinking water of rodents. Fund. Appl. Toxicol. 17:347-360.
Species	rat
Strain	Fischer 344

Sex	male/female
Route of Administration	drinking water
Exposure Period	14 days and 13 weeks
Frequency of Treatment	ad libitum
Post Exposure Observation Period	none
Doses	14-day: 0.5, 1.0, 2.0, 5.0, 10%; 5/sex/dose level. 13-week: 0.25, 0.5, 1.0, 2.0, 5.0%; 10/sex/dose level.
Control Group	Yes
Method	OECD Guideline 407 OECD Guideline 408 was used for
GLP	yes
Test substance	as prescribed by 1.1-1.4
Remark	Rats, 6-7 weeks old at start of the study, were housed 5 per cage. Drinking water containing acetone and NIH 07 feed were provided ad libitum. The time-weighted average doses were: 14-day males, 714, 1616, 2559, 4312, and 6942 mg/kg; 14-day females, 751, 1485, 2328, 4350, 8560 mg/kg; 13-week males, 200, 400, 900, 1700, and 3400 mg/kg; 13-week females, 300, 600, 1200, 1600, and 3100 mg/kg. Body weights were determined weekly and water consumption twice weekly. At necropsy, liver, right kidney, right testis, heart, thymus, brain, lungs, and, at 13 weeks only, spleen were taken for determination of weights and histopathology. Blood samples were obtained before the 13-week sacrifice for measurement of hematological indices. Male reproductive endpoints were assessed, and stage and length of the estrous cycle were evaluated in females.
Remark	NOEL was 2% for 14-day (males: 2%, 2559 mg/kg; females: 5%, 4350 mg/kg); 1% for 13-week (males: 1%, 900 mg/kg; females: 5%, 3100 mg/kg). LOEL was 5% for 14-day (males: 5%, 4312 mg/kg; females: 10%, 8560 mg/kg); 2% for 13-week (males: 2%, 1700 mg/kg).
Result	No deaths were seen during the study. Water consumption, and thus the acetone dose, was reduced in rats given 5% or greater level of acetone. Body weights were depressed in male and female rats given 5 or 10% acetone in both the 14-day and 13-week studies. There were no treatment-related clinical toxic signs during the studies. During the 13-week study, relative kidney (both sexes), liver (both sexes), and testis weights were found in the 2 and 5%

groups. Similar increases were reported to have occurred in the 14-day study at the same or lower doses (numbers not given). Hematological effects included mild lymphocytosis in male rats at 2% and male and males at 5%, decreased erythrocyte counts and hemoglobin levels at 2 and 5% and reticulocyte counts at 0.5% in male rats, and increased mean corpuscular hemoglobin and mean cell volume at 1% and higher in males and in 5% females. Platelet counts were mildly depressed in males and females in the 5% dose groups. Histopathologic lesions included bone marrow hypoplasia in 5 of 5 male rats given 10% acetone in the 14-day study. Dose-related increases in the incidence and severity of nephropathy, similar to that seen in aging rats, were seen in male rats. Minimal-to-mild splenic pigmentation was seen in male rats at the 2% and 5% dose levels in the 13-week studies. Acetone exposure of male rats for 13 weeks resulted in depressed sperm motility, cauda epididymal weight, and epididymal weight and an increased incidence of abnormal sperm. There was no indication of changes in vaginal cytology suggestive of changes in the estrous cycle.

Reference	Dietz, D.D., Leininger, J.R., Rauckman, E.J., Thompson, M.B., Chapin, R.E., Morrissey, R.L., and Levine, B.S. (1991). Toxicity studies of acetone administered in the drinking water of rodents. Fund. Appl. Toxicol. 17:347-360.
Species	rat
Strain	Sprague-Dawley
Sex	male/female
Route of Administration	gavage
Exposure Period	93, 94, or 95 days (interim sacrifice at 46 or 47 days)
Frequency of Treatment	once/day
Post Exposure Observation Period	1 day
Doses	100, 500, 2500 mg/kg; 30 M/30 F per dose level
Control Groups	yes
Method	OECD Guideline 408
GLP	yes
Test substance	as prescribed by 1.1-1.4
Remark	Thirty male and 30 female 31-day-old rats were housed individually. Animals were dosed once/day by oral gavage with solutions of 0, 1.0, 5.0, or 25% acetone in reagent grade water. Dosing volumes were adjusted weekly for

body-weight changes. Animals were dosed for 46-47 days (interim sacrifice) or 93-95 days (final sacrifice). Retroorbital blood samples and urine were collected prior to interim sacrifice of 10 males and 10 females from each group at 46-47 days and 20 males and 20 females from each group at 94-96 days (one day after end of dosing period). Ophthalmic examinations were conducted prior to study termination. Extensive gross pathological examination was performed at necropsy at which time organs were removed for determination of weights at final sacrifice. Approximately 26 organs or tissues and all tissue masses were removed at final necropsy and prepared for histological examination.

Result

One control female (day 85), one 100 mg/kg female (day 3), two 2500 mg/kg males (days 6 and 36), and three 2500 mg/kg females (days 3, 3, and 56) died during the study; deaths of 5 of the 6 were ascribed to dosing errors. No toxicologically significant effects on body weight or food intake were seen. Clear salivation and clear salivation prior to dosing were seen in both sexes in the 2500 mg/kg group. Hemoglobin, hematocrit, and mean cell volume were significantly increased in males of the 2500 mg/kg group at the interim sacrifice. At the final sacrifice, hemoglobin, hematocrit, mean cell volume, and mean cell hemoglobin were significantly elevated in 2500 mg/kg males and hemoglobin and hematocrit in 2500 mg/kg females. Statistically sig-nificant differences at final sacrifice included decreased platelet count in 2500 mg/kg males, increased mean cell volume in 500 mg/kg females, increased alanine amino-transferase in 2500 mg/kg females at the interim sacrifice and in males at the final sacrifice, depressed glucose and potassium levels in 2500 mg/kg males at the final sacrifice. Other statistically significant and nonsignificant changes were reported in 2500 mg/kg males and females at the final sacrifice, but these were not considered toxi-cologically significant. Statistically significant organ weight changes included increased kidney weights in 500 and 2500 mg/kg females, increased kidney-to-body and -brain weight ratios for males and females in the 2500 mg/kg group, increased liver/body weight ratio in 2500 mg/kg males, increased liver weights, and liver-to-body and -brain ratios in 2500 mg/kg females, depressed brain weights in 2500 mg/kg males, and increased

	heart/brain weight ratio in 2500 mg/kg females. Histopathological findings included renal proximal tubule degeneration in control and exposed animals of both sexes and intracyto-plasmic droplets or granules (hyaline droplets) in the proximal tubular epithelium in control and exposed animals, predominantly in males. (Kidney lesions are expected components preceding the development of chronic progressive glomerulonephtopathy, a common aging syndrome in Sprague-Dawley rats.) Although the incidence levels for both of these lesions were similar in control and exposed animals, the severity of distribution was markedly altered with increasing dose. In male rats, testicular interstitial edema was seen in both control and test animals with similar incidence and severity. Reactive hyperplasia of the mesenteric and mandibular lymph nodes and splenic granular pigmentation was seen more commonly in 2500 mg/kg male rats; these increases were not statistically or biologically significant.
Reference	Mayhew, D.A. and Morrow, L.D. (1988). Ninety-day gavage study in albino rats using acetone. United States Environmental Protection Agency Contract No. 68-01-7075. American Biogenic Corporation Study 410-2313.
Species	rat
Strain	Sprague-Dawley
Sex	male
Route of Administration	inhalation
Exposure Period	2, 4, and 8 weeks
Frequency of Treatment	3 h/day, 5 days/wk
Post Exposure Observation. Period	2 weeks (following 8-week exposure only)
Doses	19,000 ppm; 9 animals (total)/time-of-exposure group
Control Group	yes
GLP	no data
Test substance	ACS Grade, Instr-Analyzed (J.T. Baker)
Remark	Groups of rats were exposed to 19,000 ppm of acetone for 3 h per day. Exposures were repeated 5 times per week for 2, 4, or 8 weeks. At 2, 4, and 8 weeks of exposure and 2 weeks postexposure, groups of 5 exposed animals and 5 controls were weighed and anesthetized (pentobarbital), and blood was withdrawn for deter-mination of serum glutamic-oxaloacetic transaminase (SGOT, lactic dehydrogenase (LDH), and blood urea nitrogen (BUN).

	The rats were killed, and the whole brain, lungs, kidneys, and liver were removed and weighed. Lungs were also weighed dry to determine fluid content, and triglyceride was determined in liver. At each time interval, 4 exposed rats and 4 controls were killed, and liver, heart, lung, kidney, and brain were taken for histopathological examination.
Result	Body weight gain was slightly, but nonsignificantly (p>0.05), depressed throughout the exposure period and 2 weeks postexposure. Brain and kidney weights were depressed during the exposure period only. Nonsignif-icant increases in SGOT (AST) were seen at 2, 4, and 8 weeks. No other effects were seen. Although body, brain, and kidney weights were depressed and SGOT was slightly elevated, there were no statistically significant findings with respect to any toxicological index meas-ured. There were no untoward histopathological findings.
Reference	Bruckner, J.V. and Peterson, R.G. (1981). Evaluation of toluene and acetone inhalant abuse. II. Model develop-ment and toxicology. Toxicol. Appl. Pharmacol. 61:302-312.

5.5 Genetic Toxicity in Vitro

Type	chromosomal aberration
System of Testing	Chinese hamster lung fibroblast cell line CHL (Cancer Research Institute: Tokyo)
Concentration	40 mg/mL
Metabolic Activation	with and without
Result	positive
GLP	no data
Test substance	no data
Remark	Cells were exposed to chemical for 24 or 48 h. Colcemid added 2 h before harvesting cells, which were trypsin-ized, suspended in hypotonic KCl for 13 min, and separated by centrifuging. The cells were fixed with acetic acid-methanol and fixed on glass slides, which were air dried. The cells were stained with Giemsa, and 100 metaphases were scored for polyploid cells and structural chromosomal aberrations.
Result	Acetone produced 6.0% polyploid cells at 48 h, and 28.0% cells with structural aberrations were at 24 h. The authors consider an incidence of less than 4.9% aberrations to be negative and greater than 10% to be positive. The dose at

	which structural aberrations were detected in 20% of the metaphases observed (D20) was 36.9 mg/mL. The authors noted that the test was positive at 48 h also, but negative in the presence of S9 mix. Control and solvent-control (saline, DMSO, ethanol, sodium carboxymethyl cellulose) incidences of aberrations were said to be 3% or less.
Reference	Ishidate, M., Jr., Sofuni, T., Yoshikawa, K., Hayashi, M., Nohmi, T., Sawada, M., and Matsuoka, A. (1984). Primary mutagenicity screening of food additives currently used in Japan. Food Chem. Toxicol. 22:623-636.

Type	chromosomal aberration
System of Testing	Chinese hamster ovary cells
Concentration	0.5-5.0 mg/mL
Metabolic Activation	with and without
Result	negative
GLP	no data
Test substance	as prescribed by 1.1-1.4
Remark	Cells were exposed to chemical for 8 h, washed to remove the test chemical, and treated with colcemid for 2.0-2.5 h before cell harvest. The method of Galloway et al., Environ. Mutagen. 7,1985 was followed except that the total duration of 10-12 h. The cells were fixed with 3:1 acetic acid-methanol and stained with 5% Giemsa on glass slides. Simple, complex, and "other" aberrations were determined on 100-200 cells. Chromatid and chromosome gaps were recorded but were not used in the analysis.
Result	Acetone produced 0-3.5% simple aberations and 0-2% complex aberations, and a total percentage of 1.5-4.0% for the three dose levels tested. The results were equal to or less than the values observed with untreated control cells.
Reference	Loveday, K.S., Anderson, B.E., Resnick, M.A., and Zeiger, E. (1990). Chromosome aberration and sister chromatid exchange tests in Chinese hamster ovary cells in vitro. V: Results with 46 chemicals. Environ. Mol. Mutagen. 16:272-303.

Type	sister chromatid exchange
System of Testing	Chinese hamster ovary cells
Concentration	0.05-5.0 mg/mL
Metabolic Activation	with and without
Result	negative
GLP	no data

Test substance	as prescribed by 1.1-1.4
Remark	Cells were exposed to chemical for 2 h before adding bromodeoxyuridine (BrdUrd), which was incubated for 24 h. After 26 h fresh medium with BrdUrd and colcemid was added for an additional 2-2.5 h at 37°C. Cells were examined for signs of toxicity (confluence in the monolayer) before harvesting. Cells were separated by centrifugation, fixed with 3:1 acetic acid-methanol, fixed on glass slides, and stained with Hoechst 33258 and then 5% Giemsa. Fifty (50) second division metaphase cells were scored for sister chromatid exchanges (SCEs).
Result	Acetone produced 8.5-8.7 SCEs per cell when tested without activation at the three dose levels examined. When tested with activation 6.4-7.5 SCEs per cell were observed. The results were equal to or less than the values observed with untreated control cells. A postive trend test with at 20% increase in chromatid exchanges with at least one dose was required for a positive response.
Reference	Loveday, K.S., Anderson, B.E., Resnick, M.A., and Zeiger, E. (1990). Chromosome aberration and sister chromatid exchange tests in Chinese hamster ovary cells in vitro. V: Results with 46 chemicals. Environ. Mol. Mutagen. 16:272-303.

Type	two-stage cell transformation assay
System of Testing	BALB/3T3 clone A31-1-1 (JCRB0601)
Concentration.	0.5%
Metabolic Activation	without
Result	negative
GLP	no data
Test substance	no data
Method	BALB/3T3 cells in culture were treated with test chem-ical (but not acetone) for 72 h. The chemical was removed, and the cells were grown in medium for 3 days. The promoter 12-O-tetradecanoylphorbol 13-acetate (TPA) or 0.5% acetone was added. After two weeks, the promoter was removed, and the cells were grown for 3 weeks at which time they were collected and stained with Giemsa.
Remark	Acetone caused no transformation when applied during the promotion phase to cells treated with DMSO. It is not clear that cells were treated with acetone alone or with acetone followed by TPA. TPA was, however, applied to the cells in acetone solution.

Reference	Sakai, A. and Sato, M. (1989). Improvement of carcin-ogen identification in BALB/3T3 cell transformation by application of a 2-stage method. Mutat. Res. 214:285-296.
Type	minimal inhibitory concentration
System of Testing	trp- E. coli, 3 strains: WP2 (wild-type, repair proficient), WP67 (uvr- polA-), and CM871 (uvrA- recA- lexA-).
Concentration.	Up to 40 mg/well
Metabolic Activation	with and without
Result	negative
GLP	no data
Test substance	no data
Method	Six replicates (rows) of eight twofold dilutions of each compound were prepared in Microtiter plates. Three rows were filled with phosphate-buffered saline and three with S9 mix. One strain of each of the three bacteria was added to each of the eight wells in one of the rows. The plates were incubated at 37°C and observed for increases in turbidity or the formation of a pellet of settled cells. Apparently positive results were confirmed by subculture on agar plates. Method is liquid micromethod modification of the rec-assay system with B. subtilis (Kada et al., 1981) and the E. coli system of McCarroll et al. (1981).
Remark	Method results in a minimal inhibitory concentration (MIC). The MIC for acetone under each condition of strain and activation (six values) was > 40 mg/well. A ratio between the MICs in repair-proficient (WP2) and repair-deficient (WP67 and CM871) strains greater than 2 was considered to be significant in the test. Although these ratios could not be obtained for acetone (since all values were "> 40 mg"), the values suggest that acetone would be an extremely weak DNA-damaging agent if it were positive. The overall accuracy for predicting car-cinogenicity for the DNA-repair test was 72.4% for a battery of 75 of the 135 compounds for which clear carcinogenicity data were available and that included several compounds reported to be nonmutagenic carcin-ogens or noncarcinogenic mutagens.
Reference	De Flora, S., Zanacchi, P., Camoirano, A., Bennicelli, C., and Badolati, G.S. (1984). Genotoxic activity and potency of 135 compounds in the Ames reversion test and in a bacterial DNA-repair test. Mutat. Res. 133:161-198.

Kada, T., Hirano, K., and Shirasu, Y. (1980). Screening of environmental chemical mutagens by the Rec-assay system with Bacillus subtilis. In: De Serres, F.J. and Hollaender, A. (Eds.). Chemical Mutagens, Vol. 6, Plenum, New York, 149-173.

McCarroll, N.E., Piper, C.E., and Keech, B.H. (1981). An E. coli microsuspension assay for the detection of DNA damage induced by direct-acting agents and promutagens. Environ. Mutagen. 3:429-444.

Type	mitotic chromosomal malsegregation, mitotic recombination, and point mutations.
System of Testing	Saccharomyces cerevisiae diploid strain D61.M
Concentration.	6.82-7.83%
GLP	no data
Test substance	no data
Remark	Chemicals were at least 97%
Results	Positive for aneuploidy; negative for mitotic recombination and point mutations.
Method	Chemicals were pipetted directly into growing cultures in peptone-glucose-yeast extract (YEPD) medium and incubated at 28°C for 4 h, placed in an ice bath for < 16 h, and then incubated at 28°C on a shaker for 4 h (cold-interruption procedure). Samples of cultures were plated on a selective cyclohexamide medium. After 6-7 days, the plates were scored for colony color and numbers. Red colonies reflect cumulative effects of events like point mutations, mitotic recombinations, and deletion of chromosomal fragments. White colonies contain presumptive monosomics; these are confirmed by establishment of a requirement for leucine.
Remark	Acetone gave inconsistent results with the original protocol, which did not have the ice-storage step. The authors found that storage in ice for 16 h or more following the initial incubation gave repeatable positive results (Zimmermann et al. 1984). Most of the cyclohexamide-resistant colonies were white and almost all of these were leucine requiring, indicating that these colonies were monosomics. Red resistant colonies did not increase and were not significantly leucine requiring, indicating that acetone did not induce point mutations or recombinations under the test conditions.

Remark

Using the method of Zimmermann et al. (1985), Mayer and Goins (1994) reported that concentrations of acetone up to 459 mM (2.7%) did not cause chromosome loss or mutations in S. cerevisiae D61.M. In an interlaboratory comparison of mitotic chromosome loss in S. cerevisiae, acetone was positive in one laboratory at levels of ca. 45-55 mg/mL using the cold-interruption procedure of Zimmermann et al. (1985) but negative in a second laboratory. Both laboratories reported acetone negative using the standard procedure with overnight incubation at 28°C (Whittaker et al., 1989). Acetone was positive for production of aneuploidy in S. cerevisiae using the cold-interruption procedure of Zimmermann et al. (1985) at levels > 40 mg/mL. It was negative using the standard procedure and did not produce other genetic effects (gene mutation, mitotic recombination, etc.) with either protocol (Albertini, 1991). The merokinetic effect (multipolarity) of acetone on chromosome division of human leukocytes was reported by Kabarity (1969). Acetone caused the formation of multiple-spindle apparatus leading to the movement of each part of the centrosome to one pole. The author concluded that star metaphases are caused by the application of high con-centrations of acetone and not by a specific effect of it.

Reference

Zimmermann, F.K., Mayer, V.W., Scheel, I., and Resnick, M.A. (1985). Acetone, methyl ethyl ketone, ethyl acetate, acetonitrile and other polar aprotic solvents are strong inducers of aneuploidy in Saccharomyces cerevisiae. Mutat. Res. 149:339-351.

Albertini, S. (1991). Reevaluation of the 9 compounds reported conclusive positive in yeast Saccharomyces cerecisiae aneuploidy test systems by the Gene-Tox Program using strain D61.M of Saccharomyces cerevisiae. Mutat. Res. 260:165-180.

Kabarity A. (1969). Wirkung von Acetone auf die Chromosomen-

Mayer V.W. and Goins, C.J. (1994). Induction of chromosome loss in yeast by combined treatment with neurotoxic hexacarbons and monoketones. Mutat. Res. 341:83-91.

Whittaker, S.G., Zimmermann, F.K., Dicus, B., Piegorsch, W.W., Fogel, S., and Resnick, M.A. (1989). Detection of induced mitotic chromosome loss in Saccharomyces cerecisiae - An interlaboratory study. Mutat. Res. 224:31-78.

Zimmerman, F.K., Mayer, V.W., and Scheel, I. (1984). Induction of aneuploidy by oncodazole (nocodazole), an anti-tubulin, and acetone. Mutat. Res. 141:15-18.

Type	DNA-cell binding
System of Testing	E. coli Q13 and ^{32}P-labeled E. coli DNA
Concentration.	50 and 500 ppm
Metabolic Activation	with and without
Result	negative
GLP	no data
Test substance	no data
Method	E. coli, [^{32}P]DNA (prepared from E. coli Q13, the test chemical, and possibly lysozyme, S9 mix, or both, were combined with TSM buffer, and the mixture was incubated at 37°C for 30 or 60 min (sometimes up to 120 min). The cells were isolated by addition of cold TSM buffer and centrifugation. The separated sediment was washed, and its radioactivity was determined by scintillation spectrometry. The incorporation of more than 1% of the total [^{32}P]DNA above the control value into the cellular pellet was taken as indicative of a positive result.
Remark	An incorporation level of 1% was equal to the statistical mean of more than 150 controls plus two standard deviations. A negative control and positive control (methyl methanesulphonate) were run. Acetone (50 ppm/500 ppm) gave levels of 0.0/0.0% (i.e., less than control), 0.2/0.2%, 0.0/0.1%, and 0.4/0.4% recovered with the pellet following incubation of cells, DNA, and acetone with no additions, with added lysozyme, with added S9, or with added lysozyme and S9, respectively.
Reference	Kubinski, H., Gutzke, G.E., and Kubinski, Z.O. (1981). DNA-cell-binding (DCB) assay for suspected carcinogens and mutagens. Mutat. Res. 89:95-136.

Type	DNA single-strand break/alkaline elution assay
System of Testing	Rat hepatocytes (strain not provided)
Concentration.	1%

Metabolic Activation	without
Result	negative
GLP	no data
Test substance	no data
Method	Volatile compounds were added to freshly harvested rat hepatocytes in sealed culture flasks; the cells were exposed for 3 h. The cells were lysed and protein removed on a Nucleopore filter, and the lysate was added to a Millipore elution column. DNA was eluted with terapropyl ammonium hydroxide solution. The time course of elution was determined by analysis of timed fractions for DNA by fluorimetric analysis, and an elution rate was calculated. Cytotoxicity to the exposed cells was determined by GOT release or by trypan blue exclusion (Bradley, M.O. et al., Cancer Res. 42,1982).
Reference	Sina, J.F., Bean, G.R., Dysart, G.R., Taylor, V.I., and Bradley, M.O. (1983). Evaluation of the alkaline elution/rat hepatocyte assay as a predictor of carcinogenic/mutagenic potential. Mutat. Res. 113:357-391.

Type	yeast gene mutation assay
System of Testing	Schizosaccharomyces pombe, P1 (ade6-60/rad10-198, h-)
Concentration.	5% acetone, 60 min.
Metabolic Activation	with and without
Result	negative
GLP	no data
Test substance	Analytical grade
Method	S. pombe (P1) cells were incubated with the chemical with or without addition of S9 mix for 1 h. A phenotypic change from red cell color to white will be induced by mutation at any of 5 loci. A doubling of the incidence of mutant (white) colonies was accepted as a positive result.
Reference	Abbondandolo, A., Bonatti, S., Corsi, C., Corti, G., Fiorio, R., Leporini, C., Mazzaccaro, A., Nieri, R., Barale, R., and Loprieno, N. (1980). The use of organic solvents in mutagenicity testing. Mutat. Res. 79:141-150.

Type	mouse lymphoma assay
System of Testing	L5178Y mouse lymphoma TK+/- 3.7.2C cells
Concentration.	10-30 mg/mL
Metabolic Activation	without
Result	negative
GLP	no data

Test substance	no data
Method	This assay depends on the mutation of trifluorothymi-dine-susceptible (TFTs) heterozygous TK+/- cells to TFT-resistant (TFTr) TK-/- cells. TK+/- cells are incu-bated for 3 h in the presence of the test compound. The cells are washed, left for 48 h, and then resuspended in soft-agar cloning medium with or without TFT. Colonies growing in the absence of TFT are used for cell survival estimation, and those growing in the presence of TFT are counted as mutant (TFTr) colonies. (Amacher, D.E. et al. Mutat. Res. 64,1979).
Reference	Amacher, D.E., Paillet, S.C., Turner, G.N., Ray, V.A., and Salsburg, D.S. (1980). Point mutations at the thymi-dine kinase locus in L5178Y mouse lymphoma cells II. Test validation and interpretations. Mutat. Res. 72:447-474.

Type	Microscreen SOS lambda prophage induction assay
System of Testing	E. coli strain WP2s (lambda); E. coli strain SR714.
Concentration.	10%
Metabolic Activation	with and without
Result	negative
GLP	no data
Test substance	no data
Method	Midexponential cell cultures of WP2 (lambda) are added to serial dilutions of the test compound, and the mixtures are incubated at 37°C for 20 h when they are scored for growth inhibition (lack of turbidity). Aliquots from sub-toxic wells are added to soft agar, a midexponential culture of the indicator strain SR714 is added, and the mixture is poured onto agar plates. Following overnight incubation at 37°C, the plates are scored for plaques. A positive result is indicated by a reproducible, dose-related ratio of plaque-forming units (PFUs) per plate for the test compound to the PFUs per plate for three controls.
Remark	Positive and negative (solvent-free) controls are run. The sensitivity of the Microscreen assay for carcinogens was claimed to be 76%, whereas the specificity was 56%. Acetone did not induce prophage lambda in the E. coli WP2s (lambda) Microscreen assay in the presence or absence of an S9 activating system (DeMarini et al., 1991). The mutagenic potencies of 2-aminoanthracene and 2-nitrofluorene were reduced when dissolved in DMSO or methanol compared to their activity when dissolved in

	acetone.
Reference	Rossman, T.G., Molina, M., Meyer, L., Boone, P., Klein, C.B., Wang, Z., Li, F., Lin, W.C., and Kinney, P.L.(1991). Performance of 133 compounds in the lambda phage prophage induction endpoint of the Microscreen assay and a comparison with S. typhi-murium mutagenicity and rodent carcinogenicity assays. Mutat. Res. 260:349-367. DeMarini, D.M., Lawrence, B.K., Brooks, H.G., and Houk, V.S. (1991). Compatibility of organic solvents with the Microscreen prophage-induction assay: solvent-mutagen interactions. Mutat. Res. 263:107-113.
Type	SOS chromotest
System of Testing	E. coli PQ37
Concentration.	40 µL/mL (32 mg/mL)
Metabolic Activation	with and without
Result	negative
GLP	no data
Test substance	no data
Method	Duplicate tubes containing 10 µL of test substance and 250 µL of bacterial suspension were incubated for 2 h. β-Galactosidase and alkaline phosphatase were then measured colorimetrically following the formation of chromophores in reactions catalyzed by the enzymes.
Remark	In E. coli PQ37, the structural gene for β-galactosidase lacZ is placed under the control of the SOS gene sfiA. The expression of this gene, induced by DNA damage, is measured directly by determination of the β-glucosidase activity in a simple colorimetric assay. The SOS induc-tion factor is the ratio of the absorbency of the β-galacto-sidase reaction product to that of the alkaline phosphatase reaction product. A result was considered positive if the SOS induction facator for the test compound exceeded that of the corresponding solvent control (ratio set at 1) by more than 0.5 and the β-galactosidase activity also increased. Positive and negative (solvent) controls were run.
Reference	Von der Hude, W., Behm, C., Guertler, R., and Basler, A. (1988). Evaluation of the SOS chromotest. Mutat. Res. 203:81-94.
Type	Salmonella typhimurium reserve mutation assay
System of Testing	TA98, TA100, TA1535, TA1537, TA1538

Concentration	not stated
Metabolic Activation	with and without
Result	negative
Method	OECD Guideline 471
GLP	no data
Test substance	Reagent grade pure compound
Reference	De Flora, S., Zanacchi, P., Camoirano, A., Bennicelli, C., and Badolati, G.S. (1984). Genotoxic activity and potency of 135 compounds in the Ames reversion test and in a bacterial DNA-repair test. Mutat. Res. 133:161-198.

Type	Salmonella typhimurium reserve mutation assay
System of Testing	TA92, TA94, TA98, TA100, TA1535, TA1537
Concentration.	10 mg/plate maximum
Metabolic Activation	with and without
Result	negative
Method	OECD Guideline 471
GLP	no data
Test substance	no data
Method	Cells cultured overnight were preincubated with the test sample with or without S9 for 20 min at 37°C before plating. The number of revertant colonies was counted after incubation at 37°C for 2 days. The result was considered positive if the number of colonies found was twice that of the appropriate control. (Method of Ames, B. et al., Mutat. Res. 31:347, 1975).
Reference	Ishidate, M., Sofuni, T., Yoshikawa, K., Hayashi, M., Nohmi, T., Sawada, M., and Matsuoka, A. (1984). Primary mutagenicity screening of food additives currently used in Japan. Food Chem. Toxicol. 22,623-636.

Type	Salmonella typhimurium reserve mutation assay
System of Testing	TA97, TA98, TA100, TA1535, TA1537
Concentration.	0.1-10 mg/plate
Metabolic Activation	with and without
Result	negative
Method	OECD Guideline 471
GLP	no data
Test substance	as prescribed by 1.1-1.4
Method	Cells cultured overnight were preincubated with the test sample with or without S9 for 20 min at 37°C before plating. The number of revertant colonies was counted after incubation at 37°C for 2 days. The result was considered

	positive if a reproducible, dose-related response occurred over the solvent control under a single activation condition in replicate trials. (Method of Haworth, S. et al., Environ. Mutagen. 5(Suppl.1):3-142, 1983). Liver S9 fractions were prepared from Aroclor 1254-induced male Sprague-Dawley rats and Syrian hamsters. Tests were carried out using both preparations at 10% and 30%.
Reference	Zeiger, E., Anderson, B., Haworth, S., Lawlor, T., and Mortelmans, K. (1992). Salmonella mutagenicity tests: V. Results from the testing of 311 chemicals. Environ. Molec. Mutagen. 19(Suppl.21):2-141.

Type	unscheduled DNA synthesis
System of Testing	Human skin T/1 keratinocytes in culture
Concentration.	Up to 10%
Metabolic Activation	without
Result	negative
GLP	no
Test substance	no data
Method	Acetone and [^{3}H] thymidine were added (0.0-10%) to wells containing T/1 keratinocytes that had been deprived of arginine (to suppress scheduled DNA synthesis) for 3 days and treated with 25 mM hydroxyurea for 2 h (to inhibit S-phase synthesis). UDS accumulated over a 24-h incubation period was determined by direct scintillation counting of acid-precipitate whole-cell radioactivity.
Remark	At concentrations above 0.6%, acetone inhibited DNA synthesis. It did not increase accumulated 24-h DNA synthesis at any level up to 10%.
Reference	Lake, R.S., Kropko, M.L., Pezzutti, M.R., Shoemaker, R.H. and Igel, H.J. (1978). Chemical induction of unscheduled DNA synthesis in human skin epithelial cell cultures. Cancer Res. 38:2091-2098.

Type	Arabidopis recessive forward mutation assay
System of Testing	Cruciferous plant Arabadopsis thaliana
Concentration.	Up to 500 mM
Metabolic Activation	without
Result	negative
GLP	no
Test substance	no data
Method	Mature seeds of the plant were exposed to acetone and the fruits from the developing plants (M_1) were examined for

	embryo mutations (M_2). One method of scoring involves estimating the frequency of M_1 plants displaying segregation in the siliques (M_2). Five consecutive fruits from the basal part of the man stem are scored. The incubation time, temperature, pH, and buffer need to kept constant for the calculation of reliable mutation frequencies.
Remark	The test conditions for acetone were not reported.
Reference	Rédei, G.P. (1982). Mutagen assay with Arabidopsis. A report of the U.S. Environmental Protection Agency Gene-Tox program. Mutat. Res. 99:243-255.

5.6 Genetic Toxicity in Vivo

Type	transplacental host-mediated cell transformation
Species	hamster
Strain	LVG:LAK, virus-free
Sex	2 pregnant females
Route of Administration	ip
Exposure Period	gestation days 10-13
Doses	3 g/kg
GLP	no
Test substance	no data
Method	Substances dissolved in acetone or other solvent were injected ip on day 10 of gestation; primary fetal cell cultures were prepared on d 13. Subcultures were prepared every 4-6 days; plating efficiency and transformation were scored at the 3rd, 5th, 6th, or 7th and 10th subcultures. These subcultures were also assayed for ability to grow in soft agar.
Result	Rat 1: 0 transformed colonies/2327 total colonies examined; Rat 2: 0 transformed/3036 examined. Nontreated controls (17 animals) had 0 transformed colonies/37,574 total examined. Known carcinogens of several different classes induced transformation rates of 0.3-2.2%.
Reference	Quarles, J.M., Sega, M.W., Schenley, C.K., and Lijinsky, W. (1979). Transformation of hamster fetal cells by nitrosated pesticides in a transplacental assay. Cancer Res. 39:4525-4533.

Type	mouse embryo cell transformation
System of Testing	AKR-NIH-Me (cell line R-616u-b)

Concentration.	0.01%
Metabolic Activation	without
Species	NIH Swiss mice
Route of Administration	sc
Result	negative
GLP	no
Test substance	no data
Method	The toxicity was initially assessed from the cloning efficiency of AKR-infected mouse embryo cells in the presence of rat embryo cells. The transformation assay was performed with 10^6 cells/plate and 7 days of incubation with acetone at 37°C. Five mice were innolulated with 10^6 acetone-treated cells and examined for tumor production 85 days after treatment.
Result	An acetone concentaration of 0.01% produced a cloning efficiency of 6-16% and was negative in the transformation assay. No tumors developed in the five mice treated with cells from the transformation assay. Acetone was used as the vehicle in further testing with other chemicals.
Reference	Rhim, J.S., Gordon, R.J., Bryan, R.J., and Huebner, Rhim, J.S., Park, D.K., Weisburger, E.K., and tumor virus. J. Natl. Cancer Inst. 52:1167-1173.

Type	rat embryo cell transformation
System of Testing	MuLV (cell line F1706 & H43)
Concentration.	0.1%
Metabolic Activation	without
Species	F344/f Mai rats (newborn)
Route of Administration	sc
Result	negative
GLP	no
Test substance	no data
Method	The toxicity was initially assessed from the reduction in cloning efficiency of AKR-infected mouse embryo cells in the presence of rat embryo cells. The transformation assay was performed with 1.5 x 10^6 cells/plate and 5-8 days of incubation with acetone at 37°C. Twelve rats were innolulated with 10^6 acetone-treated cells and examined for tumor production 90 days after treatment.
Result	An acetone concentaration of 0.1% produced a relative cloning efficiency of 100% and was negative in the transformation assay. No tumors developed in the twelve

rats treated with cells from the transformation assay. Acetone was used as the vehicle in further testing with other chemicals.

Reference Price, P.J., Suk, W.A., Peters, R.L., Martin, C.E., Biol. Med. 150:650-653.

Price, P.J., Suk, W.A., Freeman, A.E., Lane, W.T., 21:361-367.

Type	micronucleus assay 10 animals per group
Species	hamster
Strain	CHO
Sex	male/female
Route of Administration	ip
Exposure Period	12, 24, 48, and 72 h
Doses865 mg/kg	
Method	OECD Guideline 474
GLP	no data
Test substance	no data
Remark	Method of Schmid, W. (1975). Mutat. Res. 31:9-15. Ten animals per time were sacrificed at 12, 24, 48, and 72 h. One thousand polychromatic erythrocytes (PEs) per animal were scored for micronuclei. Frequency differences between test animals and controls were statistically evaluated using the tables of Kastenbaum and Bowman (Mutat. Res. 9:527-549, 1970) at a significance level of $p < 0.05$.
Result	Control value (16 animals) was 1.19% PEs with micronuclei while treated animals had PEs of 1.40, 0.70, 0.20, and 0.90 at 12, 24, 48, and 72 h, respectively. Acetone was considered negative in this assay for inducing micronuclei formation.
Reference	Basler, A. (1986). Aneuploidy-inducing chemicals in yeast evaluated by the micronucleus test. Mutat. Res. 174:11-13.

5.7 Carcinogenicity

Species	mouse
Strain	C3H
Sex	male
Route of Administration	dermal
Exposure Period	lifetime: 502 days median survival
Frequency of Treatment	3 times/week

Post Exposure Observation Period	no
Doses20 mg	
Control Group	no
GLP	no data
Test substance	as prescribed by 1.1-1.4
Method	Acetone (25 µL) applied to shaved (once/week) backs of 40 mice
Result	One animal with carcinoma, one with lymphosarcoma of skin.
Reference	DePass, L.R., Ballantyne, B., Fowler, E.H., and Weil, C.S. (1989). Dermal oncogenicity studies on two methoxysilanes and two ethoxysilanes in male C3H mice. Fund. Appl. Toxicol. 12:579-583.

Species	mouse
Strain	ICR/HA Swiss
Sex	female
Route of Administration	dermal
Exposure Period	424 days and 365 days
Frequency of Treatment	3 times/week
Post Exposure Observation Period	no
Doses0.1 mL acetone and	0.1 mL 9:1 acetone:water
Control Group	yes
GLP	no
Test substance	no data
Remark	Acetone was applied to shaved (as needed) backs of mice using micropipet 3 times/week for duration of trial.
Result	Twenty-nine mice treated with acetone were necropsied. No skin tumors were reported. In animals receiving acetone at a concentration of 0.1 mL, 7 lung papillomas, 1 undifferentiated liver tumor, and 1 forestomach papil-loma were reported. In animals receiving acetone at a concentration of 0.1 mL (9:1 acetone:water), 7 lung papillomas were reported. Among controls (249 animal), 90 lung papillomas, 6 forestomach papillomas, and 1 forestomach carcinoma were reported.
Reference	Van Duuren, B.L., Loewengart, G., Seidman, I., Smith, A.C., and Melchione, S. (1978). Mouse skin carcinogen-icity tests of the flame retardants tris(2,3-dibromopropyl) phosphate, tetrakis(hydroxymethyl)-phosphonium chlor-ide, and polyvinyl bromide. Cancer Res. 38:3236-3240.

Species	mouse
Strain	Shell: Carworth Farms No. 1 (CF1) SPF
Sex	150 M/150 F
Route of Administration	dermal
Exposure Period	2 yr
Frequency of Treatment	1/week
Post Exposure Observation Period	no
Doses	0.2 mL
Control Group	no
Year	1985
GLP	no data
Test substance	AR-grade acetone
Method	Acetone (0.2 mL) was applied to shaved backs of mice, 1x/week for 2 yr.
Result	One fibrosarcoma of skin in treatment area in 1/150 males; no other skin tumors in 150 males. Females had 0/150 with tumors in treatment of skin. In nontreatment areas: males - 1/150 fibromosarcoma; females - 1 basal-cell carcinoma, 1 squamous cell carcinoma, 4 fibro-sarcoma, 1 undifferentiated sarcoma in 150 animals.
Reference	Zakova, N., Zak, F., Froehlich, E., and Hess, R.(1985). Evaluation of skin carcinogenicity of technical 2,2-bis-(p-glycidyloxyphenyl)propane in CF1 mice. Food Chem. Toxicol. 23:1081-1089.

5.8 Toxicity to Reproduction

Type	fertility
Species	rat
Strain	Wistar
Sex	male/female
Route of Administration	drinking water
Exposure Period	6 weeks
Frequency of Treatment	Ad libitum
Premating Exposure Period	male 6 weeks female none
Duration of Test	Parturition period in rats; 20 days in this case.
Doses	Males only: 2,5-hexanedione, 0%, 0.13%, 0.25%, or 0.50%, alone or in combination with acetone (0.50%). All concentrations calculated as weight/volume.
Control Group	yes

Method	
GLP	no data
Test substance	no data
Remark	The morphological changes as well as the functional consequences for the reproduction of the testis-injuring effect of 2,5-hexanedione (2,5-HD) were evaluated in rats. The potentiation by acetone and the reversibility of the effects were also studied. Male rats were dosed for 6 weeks alone or in combination with acetone in the drinking water. During the last week of treatment the fertility of half of the treated males was studied by intro-ducing each of them to a non-treated female rat, after which the number of matings, pregnancies, and foetuses were examined. In order to evaluate the reversibility of the effect on testis the same examination was made in the other half of the males after a 10-week dose-free period. The weight and morphology of testis from all the male animals were studied.
Result	The weight of testis, testis tubuli diameter, and fertility were reduced by 2,5-HD and further reduced in groups dosed with 2,5-HD, 0.25% and 0.50% plus acetone, 0.50%. Combined administration of acetone and 2,5-HD caused a potentiation comparable to the effect of the double dose of 2,5-HD. Minor changes were reversible within the 10 week dose-free period, whereas infertility and other severe changes in the highest combined group were non-reversible with this period. The number of matings was unaffected. Acetone alone did not differ from controls in its effect on number of foetuses, weight of testis, or tubuli diameter. While acetone potentiated the testis-injuring effect of 2,5-HD in rats, it alone had no effect on any fertility endpoint measured in this study.
Reference	Larsen, J-J., Lykkegaard, M., and Ladefoged, O (1991).

5.9 Developmental Toxicity/Teratogenicity

Species	rat whole embryo culture (10.5 day)
Strain	Sprague-Dawley
Sex	male/female
Route of Administration	other
Exposure Period	48 h
Duration of Test	48 h
Doses0.1, 0.5, 2.5% (v/v).	
Control Group	yes

Method	no data
GLP	no data
Test substance	no data
Remark	Day 10.5 embryos were cultured in whole rat serum in a roller culture apparatus for 48 h when the embryo explants were observed microscopically.
Results	2.5% acetone gave 100% embryolethality and tissue deterioration. At 0.5%, decreased somite counts and significant incidences of structurally abnormal embryos, but no deaths of embryos. No effect at 0.1%
Reference	Kitchin, K.T. and Ebron, M.T. (1984). Further development of rodent whole embryo culture: Solvent toxicity and water insoluble compound delivery system. Toxicology 30:45-57

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Species	mouse
Strain	CD-1
Sex	female
Route of Administration	inhalation
Exposure Period	gestation days 6-17
Frequency of Treatment	6 h/day, 7 days/week
Duration of Test	gestation days 18
Doses(0), 440, 2200, 6600, (11,000 on gd 6) ppm	
Control Group	yes, concurrent vehicle
NOEL	Maternal Toxicity was 6600 ppm/day
NOEL	Teratogenicity was 6600 ppm/day
NOEL	Developmental Toxicity 2200 ppm/day
Method	OECD 414
GLP	yes
Test substance	as prescribed by 1.1-1.4
Remark	No effect on number of implantations/dam, on any other reproductive index, or in fetal sex ratio. Developmental toxicity seen in 6600 ppm group as a statistically significant reduction in fetal weight and as a slight, statistically significant increase in % incidence of late resorptions, but with no decrease in mean number live fetuses per litter. No increase in fetal malformations or variations was seen.
Results	Severe narcosis was observed in mice exposed at 11,000 ppm for 6 h on gestation days 6; these effects were not observed in mice exposed to 6600 ppm on gestation days 7-17. No maternal deaths or overt signs of toxicity; no treatment-related effect on maternal or similarly exposed virgin mouse body weight, on maternal uterine weight, or

	on extragestational weight gain.
Reference	Mast, T.J., Evanoff, J.J., Rommerein, R.L., Stoney, K.H., Weigel, R.J., and Westerberg, R.B. (1988). Inhalation developmental toxicology studies: Teratology study of acetone in mice and rats. Pacific Northwest Laboratory, Battelle Memorial Institute Report No. NIH-Y01-ES-70153 to NIEHS/National Toxicology Program. PNL-6768/UC-408.
Species	rat
Strain	Sprague-Dawley
Sex	female
Route of Administration	inhalation
Exposure Period	gestation days 6-19
Frequency of Treatment	6 h/day, 7 days/week
Duration of Test	gestation days 20
Doses0, 440, 2200, 11,000 ppm	
Control Group	yes, concurrent vehicle
NOEL	Maternal Toxicity was 2200 ppm/day
NOEL	Teratogenicity was 11,000 ppm/day
NOEL	Developmental Toxicity 2200 ppm/day
Method	OECD 414
GLP	yes
Test substance	as prescribed by 1.1-1.4
Results	Pregnant rats in 11,000 ppm group showed a statistically significant reduction in body weights on gd 14, 17, and 20, a cumulative weight gain from gd 14 onward, and a exposure-related decrease in uterine weight and extra-gestational weight gain. No maternal deaths were observed and a mean pregnancy rate _93% was observed in all groups. No effect on mean liver or kidney weights of dams, organ /body weight ratios, number of implantations, mean % live pups/litter, mean % resorption/litter, or fetal sex ratio. Fetal weights for the 11,000 ppm group were statistically significant reduced compared to controls. Incidence of fetal malformations were not significantly increased, although the percetage of litters with at least one pup exhibiting malformations were greater for the 11,000 ppm group than for controls (11.5 vs 3.8%). Diversity of malformations in 11,000 ppm group was greater than in lower dose groups or control. There was no increase in incidence of fetal variations, reduced ossification sites, or mean incidence of fetal variations/litter.

Results	Plasma acetone levels 30 min postexposure correlated with increasing exposure concentration. Plasma acetone levels in 440 and 2200 ppm groups fell to control levels within 17 h but were slightly elevated in 11,000 ppm group at 17 h. Plasma levels at 30 min and 17 h did not change over course of repeated exposures. Acetoacetic acid and β-hydroxybutyric acid levels were not altered during the experiment.
Reference	Mast, T.J., Evanoff, J.J., Rommerein, R.L., Stoney, K.H., Weigel, R.J., and Westerberg, R.B., (1988). Inhalation developmental toxicology studies: Teratology study of acetone in mice and rats. Pacific Northwest Laboratory, Battelle Memorial Institute Report No. NIH-Y01-ES-70153 to NIEHS/National Toxicology Program. PNL-6768/UC-408.

Species	mouse
Strain	CD-1
Sex	female
Route of Administration	gavage
Exposure Period	gestation days 6-15
Frequency of Treatment	once/day
Duration of Test	parturition plus 3 days
Doses3500 mg/kg body weight	
Control Group	yes
Method	Chernoff-Kavlock Teratogenicity Screening Test
GLP	yes
Test substance	as prescribed by 1.1-1.4
Remark	Using the ranking system of Hardin (1987), the score for acetone was 19/22, which indicates high priority for testing in a conventional developmental toxicity assay. Acetone did not cause an increase in maternal mortality (total 2/49 vs 1/50 in control; pregnant 2/33 vs 1/37). Increased weight gain by pups (0.7±0.17 vs 0.5±0.22; $p<0.001$); decreased reproductive index (24/31 vs 34/36; $p<0.05$); percent survival of pups (89 vs 96; $p<0.01$); birth weight of pups (1.4±0.11 vs 1.5±0.19; $p<0.01$). There was no effect on litter size.
Reference	EHRT (1987). Screening of Priority Chemicals for Reproductive Hazards. Environmental Health Research and Testing, Inc. Cincinnati, OH. Project No. ETOX-85-1002. Sponsor: NIOSH/NTP Report: NTIS PB89-139083.

Chernoff, N. and Kavlock, R. (1983). A teratology test system which utilizes post natal growth and viability in the mouse. In: Short-term Bioassays in the Analysis of Complex Environmental Mixtures III. Plenum Press, NY. pp. 417-427.

5.10 Other Relevant Information

Type sensory irritation

Remark RD_{50} is defined as the concentration of an airborne chemical that produces a 50% decrease inthe respiratory rate in mice. Multiples of the RD_{50} (0.001-10) can be related to an expected response in humans (Kane et al., 1979). A sensory (respiratory) irritation study in mice revealed that the RD_{50} for acetone (Fisher Certified Reagent) was 77,516 ppm (95% confidence interval 59,004-115,366 ppm) following a 10-min exposure (Kane et al., 1980). Acetone was by far the least irritating (had the highest RD_{50}) of 40 common solvents and chemicals tested (Alarie et al., 1986). An RD_{50} value of 23,480 ppm was determined using the method of Kane et al. (1980). This was more than twice the highest value among 21 other common solvents and chemicals tested (De Ceaurriz et al., 1986).

Reference

Kane, L.E., Dombroske, R., and Alarie, Y. (1980). Evaluation of sensory irritation from some common industrial solvents. Am. Ind. Hyg. Assoc. J. 41:451-455.

Alarie, Y. and Luo, J.E. (1986). Sensory irritation by airborne chemicals: A basis to establish acceptable levels of exposure. In Toxicology of the Nasal Passages, Barrow, C.S. (Ed.), Hemisphere Publishing Corporation, Washington, DC.

De Ceaurriz, J.C., Micillino, J.C., Bonnet, P., and Guenier, J.P. (1981). Sensory irritation caused by various industrial airborne chemicals. Toxicol. Lett. 9:137-143.

Kane, L.E., Barrow, C., and Alarie, Y. (1979). A short-term test to predict acceptable levels of exposure to airborne sensory irritants. Am. Ind. Hyg. Assoc. J. 40:207-229.

Type Biochemical or cellular interactions

Remark In vitro inhibition of metabolic cooperation. This assay

measures a chemical's ability to inhibit gap junction-mediated intercellular communication, specifically, the transfer of a phosphorylated metabolite of 6-thioguanine (6TG) added to a co-culture of wild type V79 (6TGs, HGPRT+) and mutant (6TGr, HGPRT-) Chinese hamster lung fibroblast cells. The chemical was added to a co-culture of 4 x 10 (to the fifth power) 6 TGs cells and 100 6TGr cells in 5 mL of medium followed by addition of 6TG, and the mixture was incubated for 3 days. The medium, without chemical, was replaced, and the plates incubated for 3-4 days more. After decanting the medium, the cells were stained with crystal violet and scored visually for growth. Positive and negative controls were run. The test was scored positive if the recovery was twice that of the negative control. Acetone roughly doubled the recovery of 6TGr cells compared to the control over a range of 50-250 µL/mL and was consid-ered positive in the test by the authors.

Reference

Chen, T.-H., Kavanaugh, T.J., Chang, C.C., and Trosko, J.E. (1984). Inhibition of metabolic cooperation in Chinese hamster V79 cells by various organic solvents and simple compounds. Cell Biol. Toxicol. 1:155-171.

Type Metabolism

Remark

Male Wistar rats were given 1% v/v acetone in their drinking water for at least 3 days. A single ip injection of 5 mmol/kg of acetone into rats given 1% acetone in their water resulted in the appearance in blood serum of 16 plus or minus 2 nmol of 1,2-propanediol/mL and 8 plus or minus 1 nmol of 2,3-butanediol/mL. Serum D-lactate increased in these rats to 77 plus or minus 36 nmol/mL from 9 plus or minus 9 nmol/mL in control rats. No detectable 1,2-propanediol or 2,3-butanediol was found in the serum of animals after acetone or saline injection not given 1% acetone in the drinking water or in rats maintained on 1% acetone in the water but injected with saline. Liver microsomes isolated from rats maintained on 1% acetone in their water contained two oxygen- and NADPH-requiring enzymes, acetone mono-oxygenase, which catalyzed acetone conversion to acetol, and acetol monooxygenase, which converts acetol to methylglyoxal. Two pathways for the metabolism of acetone were proposed:

1. Methylglyoxal pathway: acetone > acetol > methylglyoxal > glucose.
2. Propanediol pathway: acetone > acetol > 1,2-propanediol 1-lactaldehyde > 1-lactic acid > glucose.

Remark: The enzyme that converts acetone to acetol and acetol to methylglyoxal in the rabbit has been identified as ethanol-inducible cytochrome P-450 isozyme 3a. An immunochemically homologous enzyme was demonstrated to be present in rats. (Koop, D.R. and Casazza, J.P. J. Biol. Chem. 260:13607-13612. 1985).

Reference: Casazza, J.P., Felver, M.E., and Veech, R.L. (1984). The metabolism of acetone in rat. J. Biol. Chem. 259:231-236.

Type: Metabolism

Remark: Early reports that acetone was possibly metabolized to glucose by a pathway other than those involving methyl-glyoxal and lactate but involving acetate or acetyl-CoA were confirmed by Kosugi et al. (1986a). Livers from Sprague-Dawley rats in diabetic ketosis were infused simultaneously with [2-^{14}C] acetone and [2-^{13}C] lactate, and the distribution of the labels was determined in glucose. From 32-73% of the carbon-14 was found in carbons 3 and 4, whereas 8-12% of carbon 13 was found in those carbons. The remaining carbon-13 and carbon-14 were about equally distributed among carbons 1, 2, 5, and 6. When determined in vitro in hepatocytes from rats previously fed acetone or fasted, incorporation of carbon-14 from [2-^{14}C] acetone and [2-^{14}C] pyruvate into carbons 3 and 4 of glucose was 14-39% and 8-10%, respectively. When [2-^{14}C] acetone was infused into two female Sprague-Dawley or four male Wistar rats or [2-^{14}C] pyruvate was infused into rats that had been fed, fasted, given acetone in their drinking water, or were in diabetic ketosis, 37-52% of the carbon-14 from acetone and 8-14% from pyruvate was found in glucose carbons 3 and 4. Rats in diabetic ketosis transformed [2-^{14}C] acetone partially into [1,3-^{14}C]hydroxybutyrate. The authors concluded that acetone is metabolized in rats to a large extent by a pathway in which lactate or its metabolic equivalent is not an intermediate, and that pathway is via acetyl-CoA.

Remark: In a follow-up study, Kosugi, et al. (1986b) infused [^{14}C] acetone into rats that had been fed or fasted in trace quantities or in larger quantities that resulted in blood

acetone concentrations of at least 4 mM. Under all conditions studied, that is, in rats chronically exposed to acetone, fed, or fasted, normal or diabetic, when given the trace dose, over 80% of the carbon-14 label was found in carbons 1, 2, 5, and 6 of glucose. When given the large dose, however, approximately 50% of the carbon-14 was found in glucose carbons 3 and 4. Thus, the major determinant of the pathways followed by acetone when it is metabolized is its concentration and not the prior dietary state of the animal or its prior exposure to acetone. Thus, at high acetone levels the acetate (or acetyl-CoA) pathway of acetone metabolism predominates. There is, however, no net synthesis of glucose from acetone by this pathway.

Remark: Using perfused livers from starved (48 h) male Sprague-Dawley rats, Gavino et al. (1987) identified the product of acetone metabolism in their system as largely free acetate. They perfused livers with [2-^{14}C] acetone nad isolated free [1-^{14}C] acetate from the perfusion medium but found no labeled lactate or 3-hydroxybutyrate.

Reference: Kosugi, K., Chanframouli, V., Jumaran, K., Schumann, W., and Landau, B.R. (1986). Determinants in the pathways followed by the carbons of acetone in their conversion to glucose. J. Biol. Chem. 261:13179-13181.

Kosugi, K., Scofield, R.F., Chandramouli, V., Kumaran, K., Schumann, W., and Landau, B.R. (1986). Pathways of acetone metabolism in the rat. J. Biol. Chem. 261:3952-3967.

Gavino, V.C., Somma, J., Philbert, L., David, F., Garneau, M., Bélair, J., and Brunengraber, H. (1987). Production of acetone and conversion of acetone to acetate in the perfused rat liver. J. Biol. Chem. 262:6735-6740.

Type: Metabolism

Remark: Deposition of acetone was assessed in the surgically isolated upper respiratory tracts (URTs) of male B6C3F1 /CrlBR mice (Morris, 1991). Mice were exposed to acetone at concentrations of 1.5-20 mg/L in a nose-only inhalation chamber, and air was withdrawn through a tube that had its tip placed at the larynx. Metabolism of acetone was measured in vitro in pooled homogenates of the entire nasal mucose (olfactory + respiratory tissue) from several mice.

Homogenates with added NADP and glucose-6-phosphate were incubated with varying amounts of acetone for 30 min at 37°C.

Remark: Deposition efficiency was measured at flow rates of 21, 33, or 70 mL/min and averaged 25, 20, and 14%, respectively (significantly different from each other at $p<0.01$). Deposition efficiencies were, however, similar at all acetone concentrations, which suggests that metabolism was not saturated, thus indicating that acetone was not metabolized when inspired. Acetone was metabolized by nasal homogenates via an NADPH-depen-dent pathway with a Vmax of 12 µg/min per whole nose and an apparent Km of 72 µg/mL. Kinetic analysis of deposition data showed that metabolism rates of inspired acetone were only a small fraction of that measured in vitro, suggesting that in vitro data cannot be directly extrapolated to the in vivo setting.

Remark: Using the same procedure and identical conditions, Morris and Cavanagh (1986, 1987) and Morris et al. (1986) measured acetone deposition in the upper respiratory tracts of rats, hamsters, and guinea pigs. Deposition efficiencies were in the order of Sprague-Dawley rats > B6C3F1 mice = F344 rats >Hartley guinea pig = Syrian hamster (groups significantly different from each other at $P < 0.005$). Acetone was not significantly metabolized in the upper respiratory tissues of rats, hamsters, or guinea pigs. Thus, the differences in deposition efficiencies may be the result of species-specific variations in URT perfusion rates.

Reference: Morris, J.B. (1991). Deposition of acetone vapor in the upper respiratory tract of the B6C3F1 mouse. Toxicol. Lett. 56:187-196.

Morris, J.B. and Cavanagh, D.G. (1986). Deposition of ethanol and acetone vapors in the upper respiratory tract of the rat. Fund. Appl. Toxicol. 6:78-88.

Morris, J.B. and Cavanagh, D.G. (1987). Metabolism and deposition of propanol and acetone in the upper respiratory tract of the hamster. Fund. Appl. Toxicol. 9:34-40.

Morris, J.B., Clay, R.J., and Cavanagh, D.G. (1986). Species differences in upper respiratory tract deposition of acetone and ethanol vapors. Fund. Appl. Toxicol. 7:671-

680.

Type Neurotoxicity

Remark

Garcia et al. (1978) used a variable-interval (VI) lever-pressing food-reward method to study the effects of solvents on the central nervous system in Holtzman-Dawley rats. Rats from a group of 8 trained on the VI schedule were exposed to acetone levels of 25-100 ppm for 2 h; one week elapsing between trials with any one rat. Differential effects on response rates were seen at concentrations of 35-100 ppm; although one rats showed a 3.4-fold increase in response time at a level of 50 ppm, 11 of 12 other trials over the range of 35-100 ppm resul-ted in response times of 1.0 to 1.8 times the preexposure time. In a subsequent study, Geller et al. (1979a) used a multiple fixed-ratio, fixed-interval (FR-FI) schedule of reinforcement. Three rats were exposed to 150 ppm of acetone for intervals of 0.5, 1, 2, or 4 h. Acetone produced minimal changes on FR-FI responding in 0.5 h. While both FR and FI rates increased during the 1-h exposure, they both dropped below the control value during the 2-h exposure. Variable results were obtained during the 4-h exposure. Thus, an initial increase in FR and FI rates during short exposures was followed by a decrease at longer exposures. Geller et al. (1979b) exten-ded this work to the study of the effect of acetone on a complex operant discrimination (match-to-sample) task in juvenile baboons. Baboons were exposed to 500 ppm of acetone for 24 h/day for 7 days. An increase in response time to the task was seen, although only a minimal decrease (1-4%) occurred in the number of correct responses. An increased variability was, however, seen in the number of erroneous responses.

Reference

Garcia, C.R., Geller, I., and Kaplan, H.L. (1978). Effects of ketones on lever-pressing behavior of rats. Proc. West Pharmacol. Soc. 21:433-438.

Geller, I., Hartmann, R.J., Randle, S.R., and Gause, E.M. (1979). Effects of acetone and toluene vapors on multiple schedule performance of rats. Pharmacol. Biochem. Behav. 11:395-399.

Geller, I., Gause, E., Kaplan, H., and Hartmann, R.J. (1979). Effects of acetone, methyl ethyl ketone and methyl

isopropyl ketone on a match-to-sample task in the baboon. Pharmacol. Biochem. Behav. 11:401-406.

Type Neurotoxicity

Remark: Outbred male ARS/Sprague-Dawley rats 4-14 weeks of age were exposed for varying periods of time up to 3 h to levels of 12,600 to 50,600 ppm of acetone. CNS depression and narcosis were evaluated by a battery of simple tests of unconditioned performance and reflexes.

Remark: The degree of CNS depression and rapidity of its induc-tion were dependent on the concentration of acetone. Performance scores of rats exposed to 12,600-25,300 ppm decreased linearly up to 3 h; 50,600 ppm of acetone was lethal to the rats in 2 h. After the 3-h exposure to 19,000 ppm of acetone, preexposure performance was attained in 9 h, but after exposure to 25,300 ppm preex-posure performance was not attained until 21 h had elapsed.

Reference: Bruckner, J.V. and Peterson, R.G. (1981). Evaluation of toluene and acetone inhalant abuse I. pharmacology and pharmacodynamics. Toxicol. Appl. Pharmacol. 61:27-38.

Type Neurotoxicity

Remark: The neurotoxic effects of several aliphatic ketones and related compounds on peripheral nerves were studies in Donryu rats by evaluation of neurological signs and measurement of maximum conduction velocities of motor and sensory fibers in the tail. Acetone was injected sc into 4 rats at a dose level of 400 mg/kg per day, 5 days/week, for 15 weeks (total 7.1 g/animal). Acetone injected sc had no effect on growth and produced no neurological signs (dullness in movement, difficulty in walking, or paralysis of hind limbs) over the course of the study. Acetone injected sc had no significant effect on motor conduction velocity or on sensory conduction velocity. Compounds related to 2-hexanone demonstrated neurophysiological signs and significant effects on conduction indices.

Reference: Misumi, J. and Nagano, M. (1984). Neurophysiological studies on the relationship between the structural properties and neurotoxicity of aliphatic hydrocarbon compounds in rats. Br. J. Ind. Med. 41:526-532.

Type Neurotoxicity

Remark: Conditioned avoidance-escape behavior was studied in

female rats (Carworth Farms Elias derived) exposed to solvents using a modification of the pole-climb method of Cook and Weidley (Behavioral effects of some psycho-pharmacological agents. Ann. N.Y. Acad. Sci. 66:740, 1957). Groups of 8 rats were exposed to 3000, 6000, 12,000 or 16,000 ppm of acetone, 4 h/day, 5 days/week, for 10 exposure days. Animals were tested for avoidance and escape behavior before and immediately after an exposure period. Exposure of rats to 3000-16,000 ppm of acetone had no effect on growth. Concentrations of 12,000 and 16,000 ppm produced ataxia in several animals after a single exposure; a rapid tolerance devel-oped, however, and this effect was not seen on the second or subsequent days. Specific alteration of avoid-ance behavior was seen with concentrations of 6000 ppm and above and was also associated with development of tolerance in most of the rats, only 2 of 8 at 16,000 ppm showing an avoidance response on days 4-10.

Reference: Goldberg, M.E., Johnson, H.E., Pozzani, U.C., and Smyth, H.F., Jr. (1964). Effect of repeated inhalation of vapors of industrial solvents on animal behavior I. Eval-uation of nine solvent vapors on pole-climb performance in rats. Am. Ind. Hyg. Assoc. J. 25:369-375.

Type: Neurotoxicity

Remark: De Ceaurriz et al. (1984) used the decrease in duration of immobility in a behavioral despair swimming test to measure the effect of short-term inhalation of solvents on neurobehavioral response in Swiss OF1 mice. Mice were exposed for 4 h to various concentrations of acetone or other solvents and then placed in a cylinder containing water. The proportion of time spent immobile (versus intense swimming activity) in 3 min was recorded; the time spent immobile was found to decrease with increasing solvent concentration. The median active level (MAL), i.e., the level that produced a 50% decrease in immobility (ID_{50} value), was 2800 ppm. This level was compared to the MAL for sensory irritation (RD_{50} value), which has been variously reported as 77,516 ppm (Kane et al., 1980) and 23,480 ppm (DeCeaurriz et al., 1981). The results suggest that neurobehavioral effects may be a more sensitive indicator of exposure than sensory irritation.

. Reference: De Ceaurriz, J., Micillino, J.C., Marignac, B., Bonnet, P.,

Muller, J., and Guenier, J.P. (1984). Quantitative evaluation of sensory irritating and neurobehavioral properties of aliphatic ketones in mice. Food Chem. Toxicol. 22:545-549.

Kane, L.E., Dombroske, R., and Alarie, Y. (1980). Evaluation of sensory irritation from some common industrial solvents. Am. Ind. Hyg. Assoc. J. 41:451-455.

De Ceaurriz, J.C., Micillino, J.C., Bonnet, P., and Guenier, J.P. (1981). Sensory irritation caused by various industrial airborne chemicals. Toxicol. Lett. 9:137-143.

Type Absorption from respiratory tract.

Remark: Anesthetized mongrel dogs (12-26 kg) were exposed to acetone at concentrations of 0.36 to 0.80 mg/L in air through the mouth using a tightly fitting mask fitted with a two-way valve. In addition, acetone was supplied to the lower respiratory tract only using an endotracheal tube or to the upper tract only after severing the trachea just above the bifurcation and using a syringe to collect and redirect the air back through the trachea. In the total tract retention experiments, uptake of acetone was 52% (range 50.4-54.2%) at ventilation rates between 5 and 18 breaths/min. At higher ventilation rates, the uptake values were significantly lower (42% at 21-40 breaths/min). The uptake increased with acetone concentration: at 10-15 breaths/min the uptakes were 52.1% at 0.46-0.58 mg/L, 52.9% at 0.59-0.72 mg/L, and 58.7% at 1.35-1.75 mg/L (high concentration significantly different from lower two at $p < 0.01$). At respiratory rates of 4-18 breaths/min the uptake of ca. 57% (range 50.7-59.6%) by the upper respiratory tract was greater than the uptake of ca. 49% (range 46.4-52.4%) for the lower tract.

Reference: Egle, J.L., Jr. (1973). Retention of inhaled acetone and ammonia in the dog. Am. Ind. Hyg. Assoc. J. 34:533-539.

Type Absorption and physiological effect.

Remark: Acetone levels in the blood of 200-240 g male Sprague-Dawley rats given 0.5-3% acetone in the drinking water for 7 days was linearly related to dose (2.6 mM/% in water). Rats fed 5% acetone in the drinking water attained a level of 15.9 mM (3.2 mM/% in water) in the blood in 7 days.

Acetone was irreversibly converted sequentially to acetol and 1,2-propanediol. Insulin-stim-ulated glucose oxidation was inhibited (30-40%) by acetone and acetol, but not 1,2-propanediol, in epidid-ymal adipose tissue and in isolated adipocytes from rats fed the respective compound for 7 days.

Reference: Skutches, C.L., Owen, O.E., and Reichard, G.A., Jr. (1990) Acetone and acetol inhibition of insulin-stimulated glucose oxidation in adipose tissue and isolated adipocytes. Diabetes 39:450-455.

Type: Neurotoxicity

Remark: Sprague-Dawley rats (3) were given acetone in the drinking water at a concentration of 0.5% for 8 weeks followed by 1.0% for 4 weeks. Other rats were given diols, dialdehydes, or diketones having 4 to 7 carbon atoms for 7 to 14 weeks. Acetone-dosed rats showed a normal rate of weight gain and normal clinical signs. On histological examination, no pathological changes were seen in the cervico-medullary junction of the spinal cord or the posterior tibial nerve proximal to the calf muscle branch, areas known to exhibit early changes in distal axonopathies. No differences from controls were seen in the cerebellar vermis, thoracic, lumbar, or sacral spinal cord, L5 and L6 dorsal and ventral roots and spinal ganglia, or three levels of the sciatic nerve and the plantar nerves in the hindfeet. 2,5-Hexanedione- and 2,5-hexanediol-dosed rats showed in vivo signs of symmetrical peripheral neuropathy. Histology of these rats showed extensive pathological changes in the CNS and peripheral nervous system.

Reference: Spencer, P.S., Bischoff, M.C., and Schaumburg, H.H. (1978). On the specific molecular configuration of neurotoxic hexacarbon compounds causing central-peripheral distal axonopathy. Toxicol. Appl. Pharmacol. 44:17-28.

Type: Immunotoxicity

Remark: The popliteal lymph node (PLN) assay has been proposed as a tool to predict in rodents xenobiotics likely to induce autoimmune reactions in humans. To validate this assay, histologic changes in PLNs from rats injected with acetone and other substances were compared to a local graft-versus-host GvH reaction. Acetone was included as a primary

	irritant that might interfere with the assay. Acetone, 50 µL, or other compound was injected into one hindfoot pad of BN rats, while the contralateral hind foodpad received 50 µL of saline. Local GvH reaction was induced in other BN x LW F1 rats. After 7 days, the rats were killed, the PLNs were removed, degreased, and weighed, and the PLNs were fixed and stained for histological examination.
Results	Weight indices showed that acetone significantly ($p<0.05$) increased the weight of the PLNs as did the positive reference compounds streptozotocin (STR) and diphenylhydantoin (DPH) and as did rats with a local GvH (all $p<0.01$). In contrast, however, to PLNs from STR- and DPH-treated rats, which showed specific morphological changes such as blurring of lymph node architecture, immunoblastic hyperplasia with paracortical areas, marked development of germinative centers, and medullary plasmocytosis, PLNs from acetone-treated rats showed no morphologic differences compared to the controls. Thus, while acetone produces a false-positive response in increasing PLN weight, it does not produce aberrant PLN morphology and is thus unlikely to induce autoimmunelike reactions in humans.
Reference	Brouland, J.-P., Verdier, F., Patriaarca, C., Vial, T., and Descotes, J. (1994). Morphology of popliteal lymph node response in brown-Norway rats. J. Toxicol. Environ. Health 41:95-108.
Type	Cutaneous toxicity
Remark	The isolated perfused porcine skin flap, an alternative animal model that has been used to study percutaneous absorption and cutaneous toxicity, was used to evaluate the effect of organic solvents on biochemical viability parameters, vascular response, and epidermal morph-ology. Acetone (ACS Reagent Grade) was applied topic-ally at a rate of 200 µL/5 cm^2 to skin flaps obtained from weanling, female Yorkshire pigs. The non-occluded skin samples were perfused for 8 h following dosing. Cumul-ative glucose utilization (CGU), the ratio of lactate pro-duction to glucose utilization (L/CGU ratio), and the leakage of lactate dehydrogenase (LDH) were used as biochemical indicators of alterations in glucose metab-olism and flap viability. CGU for acetone-treated skin did not differ significantly from that of the controls, and the rates of

change of glucose utilization were virtually the same. Leakage of LDH in acetone-treated skin was slightly increased over that of the control (not significant at p=0.05). Acetone caused a decrease (not significant at p=0.05) in the vascular resistance in the terminal phase of perfusion. Light microscopy showed a moderate incre-ase in intracellular edema in acetone-treated skin, but transmission electron microscopy did not show ultrastruc-tural changes. Acetone thus had only minimal effects on skin viability and other indices measured in this test.

Reference: King, J.R. and Monteiro-Riviere, N.A. (1991). Effect of organic solvent vehicles on the viability and morphology of isolated perfused porcine skin. Toxicology 69:11-26.

Type: Enzyme induction: cytochromes P-450

Remark: Male New Zealand White rabbits were untreated or given 1% (v/v) acetone in the drinking water for 10 days (Koop et al., 1985). The rabbits were fasted for 12-24 h and killed 24 h after the end of dosing. Liver micro-somes were isolated and assayed for P-450 isozyme 3a-catalyzed oxidation of 1-butanol to butyraldehyde. P-450 isozyme 3a was quantitated following separation by the immunoblotting technique and immunochemical detec-tion. Acetone increased the proportion of P-450 isozyme 3a from about 5% in control animals to 27%; acetone was the most potent of six inducers assayed (acetone> imidazole > ethanol > pyrazole > trichloro-ethylene > isoniazid). Isozyme 3a dependent butanol-oxidation activity increased proportionally with increased isozyme content.

Reference: Koop, D.R., Crump, B.L., Nordblom, G.D., and Coon, M.J. (1985). Immunochemical evidence for induction of the alcohol-oxidizing cytochrome P-450 of rabbit micro-somes by diverse agents: Ethanol, imidazole, trichloro-ethylene, acetone, pyrazole, and isoniazid. Proc. Nat. Acad. Sci. 82:4065-4069.

Type: Enzyme induction: cytochromes P-450

Remark: Microsomes from male Sprague-Dawley rats chronically treated with acetone (1% in drinking water for 10-12 days) displayed an increase in interaction with iron followed by elevated oxygen radical generation (assessed by rates of lipid peroxidation, hydroxyl (OH) radical generation, and chemiluminescence (Puntarulo and Cederbaum, 1988).

There was a twofold increase in the microsomal content of cytochrome P-450 and in the activity of NADPH-cytochrome-P-450-reductase. The authors concluded that increased oxygen radical gener-ation by microsomes after chronic acetone treatment reflects increases in enzymes of the mixed-function oxidase system.

Reference: Puntarulo, S. and Cederbaum, A.I. (1988). Increased microsomal interaction with iron and oxygen radical generation after chronic acetone treatment. Biochem.Biophys. Acta 964:46-52.

Type: Enzyme induction: cytochromes P-450

Remark: Microsomes isolated from male Sprague-Dawley rats orally intubated with acetone (5 mL/kg) on two con-secutive days and killed 24 h later had increased levels of cytochrome P-450j (9-fold increase) and cytochrome P-450b (10-30-fold increase) (Johansson et al., 1988). Results suggested that P-450b was induced mainly at the transcriptional level, whereas P-450j seemed to be regul-ated mainly by a post-transcriptional mechanism. Thus, acetone effects on metabolism of other compounds are caused by the induction of P-450 forms belonging to at least two gene subfamilies. The regul-ation of ethanol-inducible and phenobarbital-inducible P-450's (P4502E1 and P-4502B1, respectively) was reported on by Ronis et al. (1991).

Reference: Johansson, I., Ekström, G., Scholte, B., Puzycki, D., Jörnvall, H., and Ingelman-Sundberg, M.(1988). Ethanol-, fasting-, and acetone-induced cytochromes P-450 in rat liver: regulation and characteristics of enzymes belonging to the IIB and IIE gene subfamilies. Biochemistry 27:1925-1934.

Ronis, M.J., Johansson, I., Hultenby, K., Lagercrantz, J., Glaumann, H., and Ingelman-Sundberg, M. (1991). Acetone-regulated synthesis and degradation of cytochrome P4502E2 and cytochrome P4502B1 in rat liver. Europ. J. Biochem. 198:383-389.

Type: Enzyme induction: cytochromes P-450

Remark: Administration of a single dose of acetone (870 mg/kg in corn oil) by oral intubation increased the levels of cytochromes P-450IIE1 (59%; significant at $p<0.05$) and P-450IIB1 (37%; not significant) (Brady et al., 1989).

Chloroform metabolism was elevated threefold. Acetone was less effective than 2-butanone and 2-hexa-none in inducing P-450IIE1 and P-450IIB1 isozymes.

Reference: Brady, J.F., Li, D., Ishizaki, H., Lee, M., Ning, S.M., Xiao, F., and Yang, C.S. (1989). Induction of cyto-chrome P450IIE1 and P450IIB1 by secondary ketones and the role of P450IIE1 in chloroform metabolism. Toxicol. Appl. Pharmacol. 100:342-349.

Type: Enzyme induction: cytochromes P-450

Remark: Male Syrian golden hamsters administered 8% acetone in the drinking water for seven days had significantly elevated cytochrome P-450 and cytochrome b5 levels in liver microsomes as shown by induction of monooxygen-ase activities toward aniline, N-nitrosodimethylamine, 7-ethoxycoumarin, benzphetamine, and benzo[a]pyrene (Ueng et al., 1991). In the kidneys, pretreatment with acetone increased microsomal contents of the hemepro-teins and monooxygenase activities toward aniline, N-nitrosodimethylamine, and 7-ethoxycoumarin but not benzphetamine or benzo[a]pyrene. In the lungs, treatment with acetone increased aniline hydroxylase activity without affecting levels of N-nitrosodimethylamine demethylase or cytochromes P-450 and b5. Acetone treatment also markedly decreased lung microsomal benzo[a]pyrene hydroxylase and 7-ethoxycoumarin O-deethylase activities. Acetone treatment enhanced the intensity of protein bands in the P-450 molecular weight region on gel electropherograms. The results indicated that acetone induced cytochrome P-450 IIE1 in several tissues of the hamster.

Reference: Ueng, T.-H., Tsia, J.-N., Ju, J.-M., Ueng, Y.-F., Iwasaki, M., and Guengerich, F.P. (1991). Effects of acetone administration on cytochrome P-450-dependent monooxygenases in hamster, liver, kidney, and lung. Arch. Toxicol. 65:45-51.

Type: Enzyme induction: cytochromes P-450

Remark: Acetone given to Wistar rats by oral gavage (870 mg/kg on 3 days) increased the microsomal apoprotein levels of P-4501A2, P450B1/2, and P-4502E1 but was not respon-sible for the diabetes-induced increases in P-4503A1 and P-4504A1 proteins (Barnett et al., 1992).

Reference
Barnett, C.R., Petrides, L., Wilson, J., Flatt, P.R., and Ionnides, C. (1992). Induction of rat hepatic mixed-function oxidases by acetone and other physiological ketones: their role in diabetes-induced changes in cytochrome P450 proteins. Xenobiotica 22:1441-1450.

Type
Enzyme induction: cytochromes P-450

Remark
Acetone, a substrate for P-450 2E1-catalyzed oxidation in vitro, has been shown to be a substrate of P-450 2E1 in Sprague-Dawley rats (Chen et al., 1994). Following single or repeated application (oral gavage) of the P-450 2E1 inhibitor diallyl sulfide, nonfasted rats showed higher levels of acetone (6-9-fold) in blood than did controls. N-Nitrosodimethylamine demethylase activity and P-450 2E1 content of liver microsomes were suitably decreased.

Reference
Chen, L., Lee, M., Hong, J.-Y., Huang, W., Wang, E., and Yang, C.S. (1994). Relationship between cyto-chrome P-450 2E1 and acetone catabolism in rats as studies with diallyl sulfide as an inhibitor. Biochem. Pharmacol. 48:2199-2205.

Type
Enzyme induction/inhibition

Remark
Acetone injected ip into guinea pigs at 1500 and 3000 mg/kg failed to increase serum ornithine carbamyl transferase, an enzyme found primarily in the liver and whose presence in the bloodstream is indicative liver cell rupture (DiVincenzo and Krasavage, 1975). Liver damage was not seen, however, on histological exam-ination, although moderate lipid deposition was found.

Reference
DiVincenzo, G.D. and Krasavage, W.J. (1975). Serum ornithinecarbamyl transferase as a liver response test for exposure to org

Type
Ocular toxicity

Remark
Acetone (96% in water) was instilled in the eyes of anesthetized Chinchilla rabbits (Bolkova and Cejkova, 1983). The rabbits were killed at 1, 4, 7, 14, and 28 days, and the eyes were collected for biochemical and histological investigation. Alkaline phosphatase levels in the corneal epithelium were sharply elevated, reaching a peak (9 times control) in the 14-day samples but still highly elevated at 28 days. Acid phosphatase in the corneal epithelium was significantly depressed at 4 days but significantly elevated at 7 days. The levels returned to

normal by 14 days. Acetone was significantly more effective than ethanol. Alkaline and acid phosphatase levels in the corneal stroma were both significantly ($p<0.05$) depressed on the day following acetone instillation but normal at all other times. Histological examination showed that the damage to the eyes following instillation of acetone was reversible, although the epithelium had not returned to normal by 28 days.

Reference

Bolkova, A. and Cejkova, J. (1983). Changes in alkaline and acid phosphatases of the rabbit cornea following experimental exposure to ethanol and acetone: A biochemical and histochemical study. Graefe's Arch. Clin. Exp. Ophthalmol. 220:96-99.

5.11 Human Exposure

Remark

Patients with uncontrolled diabetes can have plasma acetone levels as high as 750 mg/L, which is more than 300 times the normal limit. Although the acetone levels that accompany diabetic ketoacidosis may cause persistent drowsiness and mild proteinuria, the prevailing opinion is that acetone is not responsible for the diabetic coma or any of the prominent symptoms of diabetic shock. Numerous studies have documented slight to moderate increases in breath acetone for diabetics and fasting adults. Breath acetone levels in cases of juvenile diabetes are, on average, nearly 100 times greater than normal. Diabetics who test strongly positive for glucosuria have breath acetone levels that average about 340 times above the normal limit .

Reference

Mason, M.F. and Hutson, D. (1975). The range of concentrations of free acetone in the plasma and breath of diabetics and some observations on its plasma/breath ratio. In: Proceedings of the 6th International Conference on Alcohol, Drugs, and Traffic Safety. Toronto, Canada.

Haff, A.C. and Reichard, G.A. (1977). A method for estimation of acetone radioactivity and concentration in blood and urine. Biochem. Med. 18:308-314.

Sulway, M.J. and Mulins, J.M. (1970). Acetone in diabetic ketoacidosis. Lancet I:736-740.

Sulway, M.J., Trotter, M.D., Trotter, E., and Malins, J.M.

(1971). Acetone in uncontrolled diabetes. Postgrad. Med. J. 47(Suppl.):383-387.

Siegel, L., Robin, N.I., and McDonald, L.J. (1977). New approach to determination of total ketone bodies in serum. Clin. Cl

Levey, S., Balchum, O.J., Medrano, V., and Jung, R. (1964). Studies of metabolic products in expired air. II. Acetone. J. Lab. Clin. Med. 63:574-584.

Fisher, P. (1951). The role of the ketone bodies in the etiology of diabetic coma. Am. J. Med. Sci. 221:384-387.

Rooth, G. and Östenson, S. (1966). Acetone in alveolar air, and the control of diabetes. Lancet II:1102-1105.

Stewart, R.D. and Boettner, E.A. (1964). Expired-air acetone in diabetes mellitus. New Eng. J. Med. 270:1035-1038.

Remark

Clinical findings in cases of acute intoxication suggest that acetone blood levels in excess of 1000 mg/L are necessary to cause unconsciousness in humans. Urine acetone levels ranging from 31.0-650.9 mg/L have been reported following cases of accidental or intentional exposure. An individual who consumed a paint thinning solvent that contained acetone had a breath acetone level of 2200 g/L two days after the event. A 36-h fast can result in a 40-fold elevation in breath acetone levels, which can be immediately reduced by consuming small amounts of ethanol. Acute ethanol intoxication can, however, cause a 3-10 fold rise in blood and breath acetone concentrations.

Reference

Gamis, A.S. and Wasserman, G.S. (1988). Acute acetone intoxication in a pediatric patient. Pediat. Emerg. Care 4:24-26.

Ramu, A., Rosenbaum, J., and Blaschke, T.F. (1978). Disposition of acetone following acute acetone intoxication. West. J. Med. 129:429-432.

Kobayashi, K., Okada, M., Yasuda, Y., and Kawai, S.(1983). A gas chromatographic method for the determination of acetone and acetoacetic acid in urine.

Clin. Chem. Acta 133:223-226.

Rooth, G. and Östenson, S. (1966). Acetone in alveolar air, and the control of diabetes. Lancet II:1102-1105.
Jones A.W. (1987). Breath-acetone concentrations in fasting healthy men: Response of infrared breath-alcohol analyzers. J. Anal. Toxicol. 11:67-69.

Jones A.W. (1988). Breath acetone concentrations in fasting male volunteers: Further studies and effect of alcohol administration. J. Anal. Toxicol. 12:75-79.

Neiman, J., Jones, A.W., Numminen, H., and Hillbom, M. (1987). Combined effect of a small dose of ethanol and 36 hr fasting on blood-glucose response, breath-acetone profiles and platelet function in healthy men. Alcohol Alcoholism 22:265-270.

Göschke, H. and Lauffenburger, T. (1975). Aceton in der Atemluft und Ketone im Venenblut bei vollständigem Fasten normal-und übergewichtiger Personen. Res. Exp. Med. 165:233-244.

Phillips, M., Greenberg, J., and Martinez, V. (1989). Elevated conce

Tsukamoto, S., Kanegae, T., Saito, M., Nagoya, T., Shimamura, M., Tainaka, H., and Kawaguchi, M. (1991). Concentrations of blood and urine ethanol, acetaldehyde, acetate and acetone during experimental hangover in volunteers. Jpn. J. Alcohol Drug Depend. 26:500-510.

Barz, J., Bonte, W., Keultjes, C., and Skoland, J. (1990). Concentrations of ethanol, methanol, propanol-2 and acetone in blood samples of impaired drivers. Proc. Int. Acad. Forensic Social Med. 40:49-60.

Iffland, R., Balling, M.P., Börsch, G., Herold, C., Kaschade, W., Löffler, T., Schmidtmann, U., and Stettner, J. (1994). Zur Wertung erhöhter Spiegel von GGT, CDT, Methanol, Aceton und Isopropanol im Blut alkoholauffälliger Kraftfahrer: Alkoholismusindikatoren anstelle medizinisch-psychologischer Untersuchungen?. Blutalkohol 31:273-314.

Remark	In a controlled study, at least nineteen control and twelve diabetic patients were intravenously administered 200 mL of a 0.5% solution of acetone in normal saline over 2 h. The only recorded effects were a small drop in blood pressure and a slight transient drowsiness in both treatment groups.
Reference	Koehler, A.E., Windsor, E., and Hill, E. (1941). Acetone and acetoacetic acid studies in man. J. Biol. Chem. 140:811-825.
Remark	The rate of acetone exhalation can vary over a broad range in healthy human volunteers with values typically falling between 29 and 230 mg\h. Significantly higher exhaled breath values of acetone occur for normal females compared to normal males. Exhaled acetone levels can increase and decrease rapidly in response to a loss or gain in body weight. Rapid and dramatic increases can occur when carbohydrates are removed from the diet.
Reference	Henderson, M.J. Karger, B.A. and Wrenshall, G.A. (1952). Acetone in breath. A study of acetone exhalation in diabetic and nondiabetic human subjects. Diabetes 1:188-200. Conkle, J.P., Camp, B.J., and Welch, B.E. (1975). Trace composition of human respiratory gas. Arch. Environ. Health 30:290-295.
Remark	The blood-to-air partition coefficient for acetone has been found to range between 315-350 using in vivo and in vitro techniques. The coefficient for humans declined linearly as the hematocrit was increased from 0% (plasma) to 100% (packed red blood cells). The average results for human blood ranged from a high of 315 with plasma to low of 210 with packed red blood cells. Tissue-to-air partition coefficients have also been deter-mined using human autopsy specimens consisting of muscle, kidney, lung, cerebral white matter, cerebral gray matter, fat, packed erythrocytes, and plasma. The coefficients ranged from a low of 86 for fat to a high of 217 for plasma. Most tissues had values ranging from 140-170.
Reference	Widmark, E.M.P. (1920). XXXII. Studies in the acetone concentration in blood, urine, and alveolar air. III. The

elimination of acetone through the lungs. Biochem. J. 14:379-394.

Briggs, A.P. and Shaffer, P.A. (1921). The excretion of acetone from the lungs. J. Biol. Chem. 48:413-428.

Haggard, H.W., Greenberg, L.A., and Turner, J.M. (1944). The physiological principles governing the action of acetone together with the determination of toxicity. J. Ind. Hyg. Toxicol. 26:133-151.

Fiserova-Bergerova, V. and Diaz, M.L. (1986). Determination and prediction of tissue-gas partition coefficients. Int. Arch. Occup. Environ. Health 58:75-87.

Young, I.H. and Wagner, P.D. (1979). Effect of intrapulmonary hematocrit maldistribution on O_2, CO_2, and inert gas exchange. J. Appl. Physiol. 46:240-248.

Sato, A. and Nakajima, T. (1979). Partition coefficients of some aromatic hydrocarbons and ketones in water, blood and oil. Br. J. Ind. Med. 36:231-234.

Poulin, P. and Krishnan, K. (1995). A biologically-based algorithm for predicting human tissue: Blood partition coefficients of organic chemicals. Hum. Exp. Toxicol. 14:273-280.

Remark	The rise and fall in acetone blood levels were followed after the administration of 8 to 16 g (95-135 mg/kg) of acetone to four volunteers. Administration occurred by either the oral or perianal route and no adverse effects were reported as a result of the treatment.
Reference	Widmark, E.M.P. (1919). Studies in the concentration of indifferent narcotics in blood and tissues. Acta Med. Scand. 52:87-164.
Remark	Mild-moderate eye irritant in humans.
Reference	Grant, W.M. (1986). Acetone. In Toxicology of the Eye. Charles C. Thomas, Springfield. pp. 41-42.
Remark	Approximately 10 human subjects exposed to acetone for 3-5 min were asked to classify effects on eyes, nose, and

throat. The majority of subjects reported irritation of each organ noted at 500 ppm. The majority of the subjects estimated that the maximum satisfactory concentration for 8 h would be 200 ppm.

Reference: Nelson, K.W., Ege, J.F., Ross, M., Woodman, L.E., and Silverman, L. (1943). Sensory response to certain solvent vapors. J. Ind. Hyg. Toxicol. 25:282-285.

Remark: Several test subjects drank 4.7-5.4 g (70-80 mg/kg) of acetone in water without any reported ill effects. The acetone blood levels resulting from the treatment ranged up to about 280 mg/L.

Reference: Haggard, H.W., Greenberg, L.A., and Turner, J.M. (1944). The physiological principles governing the action of acetone together with the determination of toxicity. J. Ind. Hyg. Toxicol. 26:133-151.

Remark: A self-exposure to 22 mg/L (ca. 9,300 ppm) of acetone vapor could not be tolerated for longer than five minutes due to throat irritation.

Reference: Kagan, E. (1924). Experimentelle Studien über den Einfluss technisch und hygienisch wichtiger Gase und Dämfpe auf den Organismus. XXXVI. Aceton. Arch. Hyg. Berl. 94:41-53.

Remark: Ocular contact with small amounts of acetone caused an immediate stinging sensation, but when promptly irrigated, the damage was confined to the epithelium, which was found to contain microscopic gray areas. No permanent damage resulted.

Reference: Grant, W.M. (1962). Acetone. In: Toxicology of the Eye, 1st ed., pp. 9-10. Charles Thomas, Springfield, IL.

Remark: Three cases of human corneal burns from liquid acetone reportedly healed within 48 h of irrigation and removal of the damaged corneal epithelium.

Reference: McLaughlin, R.S. (1946). Chemical burns of the human cornea. Am. J. Ophthalmol. 29:1355-1362.

Remark: Lens opacity was reportedly seen in a male patient potentially exposed to acetone while working as a painter.

Reference: Mayou, M.S. (1932). Cataract in an acetone worker. Proc. R. Soc. Med. 25:475.

Remark	No studies were located regarding death of humans after dermal exposure to acetone.
Reference	ATSDR (1994). Toxicological Profile for Acetone. US DHHS/PHS Agency for Toxic Substances and Disease Registry. Report No. TP-93/01.
Remark	Epidermal biopsy specimens were taken from the forearms of six male volunteers treated with acetone for periods of 30 or 90 min. Acetone application was found to cause cellular damage in the stratum corneum and stratum spinosum that was more severe after the 90-min treatment. Cells and the surrounding interstitial keratin layers of the stratum corneum were edematous and contained fine granular deposits. Specimens collected at 72 h post-treatment showed a high degree of repair and restoration, with some evidence of damage still present.
Reference	Lupulescu, A.P., Birmingham, D.J., and Pinkus, H. (1973). Electron microscopic study of human epidermis after acetone and kerosene administration. J. Invest. Dermatol. 60:33-45. Lupulescu, A.P. and Birmingham, D.J. (1975). Effect of lipid solvents on protein, DNA, and collagen synthesis in human skin: An electron microscopic autoradiographic study. J. Invest. Dermatol. 65:419-422.
Remark	Pretreatment of the skin with a protective gel substan-tially reduced the severity of the cellular and structural damage caused by a 90-min exposure to acetone.
Reference	Lupulescu, A.P. and Birmingham, D.J. (1976). Effect of protective agent against lipid-solvent-induced damages. Arch. Environ. Health 31:29-32.
Remark	Acetone did not affect skin barrier function when tested on skin specimens taken during three autopsies. Up to 12-min of treatment with acetone did not affect transepidermal water loss from the epidermis relative to untreated control specimens. The acetone treatment also failed to extract appreciable quantities of ceramide, fatty acids, or cholesterol from the skin.
Reference	Abrams, K., Harvell, J.D., Shriner, D., Wertz, P., Maibach, H., Maibach, H.I., and Rehfeld, S.J. (1993). Effect of

organic solvents on in vitro human skin water barrier function. J. Invest. Dermatol. 101:609-613.

Remark: Slight effects were observed when acetone was applied to the forearms of three volunteers for 15 min on 6 consecutive days. Damage to the horny layer was minimal with the water loss not exceeding 0.5 $mg/cm^2/h$.

Reference: Malten, K.E., Spruit, D., and de Keizer, M.J.M. (1968). Horny layer injury by solvents. Berufsdermatosen 16:135-147.

Remark: Four individuals removing a pool of acetone-contam-inated water from an unventilated pit were adversely affected by the vapors. Two members of the crew entered the pit to place the water in buckets, which were then hauled to the surface by the others. Before taking a lunch break, both members of the pit-crew experienced some sensory irritation and one of the members reported-ly felt inebriated. Upon returning to the pit, the latter worker fell unconscious, whereupon other members of the crew entered the pit. Upon arrival at a hospital, one employee was unconscious and another was confused, drowsy, and unsteady. The comatose individual was hospitalized for 4 days and discharged, the others were released immediately. Five of the six workers exposed to acetone vapor during the rescue operation reported feeling symptoms such as dizziness, eye and throat irri-tation, and leg weakness. The acetone vapor concentra-tion in the pit was found to be greater than 12,000 ppm.

Reference: Ross, D.S. (1973). Acute acetone intoxication involving eight male workers. Ann. Occup. Hyg. 16:73-75.

Remark: An unusual case of acetone poisoning was reported for an employee who attempted suicide by inhaling acetylene gas through a paper cup attached to a gas cylinder. He was found unconscious and was immediately taken to an emergency room where a physical examination revealed a rapid heart beat, rapid breathing, and cyanosis. Laboratory tests revealed elevations in serum glucose, creatinine, phosphorus, and lactic acid as well as hematuria, glycosuria, and ketonuria. The marked acidosis was attributed to the hypotension and hypoxia that occurred when the employee became consciousness. The acetylene

tank was found to contain liquid acetone, which acted as a carrier for the acetylene gas. The elevation in serum creatinine was considered to be the result of acetone interference with the analytical method. The author concluded that the hyperglycemia and acetonuria observed in this patient were the result of acute acetone poisoning.

Reference: Foley, R.J. (1985). Inhaled industrial acetylene. A diabetic ketoacidosis mimic. J. Am. Med. Assoc. 254:1066-1067.

Remark: An employee cleaning a kettle used to filter a synthetic fiber dissolved in acetone was reportedly overcome by the solvent vapors. The employee wore a respirator while working in the kettle; however, a poor fit resulted in a severe overexposure. The individual became unconscious while inside the kettle and was taken to a clinic while in a coma. Vomiting, salivation and hyperactivity occurred at the clinic and elevations in serum glucose and bilirubin levels were observed. Blood acetone levels 9 and 11 h after the mishap were 430 and 302 mg/L, respectively. Acetone was detected in the urine together with urobilin, red blood cells, white blood cells, and some albumin.

Reference: Sack, G. (1940). Ein Fall von gewerblicher Azeton-vergiftung. Arch. Gewerbepath. Gewerbehyg. 10:80-86.

Remark: Signs and symptoms of illness were reported for workers from three separate manufacturing sites where acetone was used in combination with other solvents. Six employees exposed to acetone at concentrations ranging from 309-918 ppm for up to 3 h over a 7-15 year period, reportedly complained of drowsiness, eye and throat irritation, dizziness, inebriation, and headache. The employees reportedly showed signs and symptoms of muscular weakness, vertigo, and chronic inflammation of the stomach, duodenum, and air passages. A physical examination showed signs of pharyngeal, conjunctival, and lung irritation in five of the six employees. The second work site employed four workers in an operation where the acetone concentrations ranged from 84-147 ppm. Workers at this site experienced nausea, abdominal pain, headache, vertigo, loss of appetite, vomiting, and other debilitating symptoms. The final site involved eleven employees and had acetone vapor concentrations ranging from 13-86 ppm. Irritation to the eyes, nose, throat, and bronchi reportedly

occurred along with severe disturbances in the central nervous system. High concentrations of carbon disulfide, a central nervous system toxicant, were also found in the last facility.

Reference: Parmeggiani, L. and Sassi, C. (1954). Occupational poisoning with acetone - Clinical disturbances, investigations in workrooms and physiopathological research. Med. Lav. 45:431-468.

Remark: Two cases of acute acetone intoxication were reported in a raincoat manufacturing operation where acetone was used in a coating to waterproof seams. In the first case, a female employee complained of stomach distress and watery eyes one morning, and was later found unconsci-ous in a bathroom. The second case followed the first by one day and was apparently less severe. The female employee reportedly fainted and convulsed at her work site but regained consciousness immediately afterwards. Samples of the workroom air revealed acetone vapor concentrations ranging from 330-495 ppm and methyl ethyl ketone concentrations ranging from about 400-560 ppm.

Reference: Smith, A.R. and Mayers, M.R. (1944). Study of poisoning and fire hazards of butanone and acetone. Ind. Bull. NYS Dept. Labor 23:174-176.

Remark: A medical survey performed on 19 men employed in a shirt factory where a 75% mixture of acetone in methanol was used to fuse collars onto shirts found that the subjects were normal in all respects except for the acetonuria that was detected. Each individual was given a through medical examination that included a neuro-logical evaluation, ophthalmology, and a complete blood count (CBC). Medical and occupational histories were also reviewed for any evidence of an occupationally induced illness. Red blood cell, white blood cell, and platelet counts were all within normal limits for each worker. Two room air samples showed peak acetone and methanol vapor concentrations of 45 and 25 ppm, respectively.

Reference: Greenburg, L., Mayers, M.R., Goldwater, L.J., and Burke, W.J. (1938). Health hazards in the manufacturing of "fused collars". II. Exposure to acetone-methanol. J. Ind. Hyg. Toxicol. 20:148-154.

Remark	A male patient attempted suicide by ingesting approximately 100 mL of a polyvinyl chloride (PVC) cement that contained cyclohexanone (39%), MEK (28%), acetone (18%), and PVC (15%). The individual also drank about 720 mL of sake (10% ethanol) 30 min before drinking the PVC solution and was comatose when admitted to the hospital about two hours later. The patient regained consciousness after about 7 h, but a persistent hyperglycemia was observed on days 1 through 6 of hospitalization. A second rise in serum glucose was then observed on days 9 through 16. Serum transaminase levels began to rise markedly on day 6 and peaked on days 12 and 13. The high concentrations of cyclohex-anone present in the blood were thought to be responsible for the coma, whereas the hyperglycemia was attributed to acetone.
Reference	Sakata, M. Kikuchi, J., and Haga, M. (1989). Disposition of acetone, methyl ethyl ketone and cyclohexanone in acute poisoning. Clin. Toxicol. 27:67-77.
Remark	An individual attempting suicide by consuming 200 mL of pure acetone was observed to be stuporous with shallow respiration when observed at the hospital one hour after the incident. He lapsed in a coma shortly after admission and his throat was red and swollen, with some tissue erosion noted on the soft palate. Complete con-sciousness was not regained until about 12 h after admission. Acetone and some albumin were present in the urine, but glucosuria was not detected. Slightly elevated blood glucose levels were observed during the first nine days of hospitalization, but liver function tests were normal. The patient reported leg pain and a marked disturbance of gait was noted when the patient became ambulatory on day six. The patient's gait slowly returned to normal. Elevated blood glucose levels were again observed about four weeks after the acetone ingestion, when the patient returned to the hospital complaining of polydypsia and polyuria. Glucose levels returned to normal after two months of dietary restriction.
Reference	Gitelson, S., Werczberger, A., and Herman, J.B. (1966). Coma and hyperglycemia following drinking of acetone. Diabetes 15:810-811.
Remark	A fatal case of intoxication occurred when an unknown amount of acetone was intentially consumed along with

acetonitrile. The acetone exposure apparently delayed the appearance of acetonitrile toxicity by inhibiting its metabolism to cyanide. The delayed toxicity obscured the diagnosis and prevented effective treatment with antidotes.

Reference: Boggild, M.D., Peck, R.W., and Tomson, C.V.R. (1990). Acetonitrile ingestion: Delayed onset of cyanide poisoning due to concurrent ingestion of acetone. Postgrad. Med. J. 66:40-41.

Remark: A patient with a history of alcohol abuse and known to be suffering from liver cirrhosis, peripheral neuropathy, cerebral atrophy, and gastrointestinal bleeding due to esophageal varices ingested acetone prior to being hospitalized. On examination, the patient was lethargic but conscious, and no throat inflammation was observed. A neurological examination gave normal results. Ketones were detected in the urine, and gastric lavage showed acetone in the stomach contents. Extremely high acetone blood levels ranging up to 2500 mg/L were also observed, but no hyperglycemia or glycosuria was reported.

Reference: Ramu, A., Rosenbaum, J., and Blaschke, T.F. (1978). Disposition of acetone following acute acetone intoxication. West. J. Med. 129:429-432.

Remark: A 2.5 year old child consumed nearly all of the fluid from a six-ounce bottle of fingernail polish remover that contained 65% acetone and 10% isopropanol. The child was unconscious when found in his home and had a seizure while being taken to a hospital. Notable clinical findings during the first 24 h included acetonuria, aceto-nemia, metabolic acidosis, respiratory depression, hypo-thermia, and hyperglycemia. Evidence of acetonuria, hyperglycemia, and an acid-base imbalance were noted on the second day. Acetone blood levels at 1, 18, 48, and 72 h after the onset of symptoms were 4450, 2650, 420, and 40 mg/L, respectively. The patient was discharged on the fourth day after a neurological examination showed no abnormalities. A 6-month follow-up examination showed no signs of neurodev-elopmental complications.

Reference: Gamis, A.S. and Wasserman, G.S. (1988). Acute acetone intoxication in a pediatric patient. Pediatr. Emerg. Care 4:24-26.

Remark

Nine other iatrogenic cases of acetone poisoning have been reported in the medical literature. The incidents generally involved hospital patients who were being treated for a broken hip or leg that required joint immobilization with a cast. Acetone was used as a setting fluid in a plaster substitute composed of poly-merized vinyl acetate, nitrocellulose, and boric acid. Both males and females were affected, and their ages ranged from about 2 to 42 years. The exposure typically occurred via vapor inhalation; however, in some cases, skin absorption was deemed to be the primary route of exposure. The onset of symptoms, typified by initial lethargy and drowsiness, occurred within 1-12 h of the exposure; nausea and vomiting were seen later. Many patients lapsed into unconsciousness, with glycosuria, and acetonuria generally observed along with an odor of acetone on the breath. Other frequently noted clinical signs and symptoms included hematemesis, labored breathing, tachycardia, and throat irritation.

Reference

Cossmann, T. (1903). Acetonvergiftung nach Anlegung eines Zelluloid-Mullverbandes. Müench. Med. Wochr. 50:1556-1557.

Strong, G.F. (1944). Acute acetone poisoning. Can. Med. Assoc. J. 51:359-362.

Chatterton, C.C. and Elliott, R.B. (1946). Acute acetone poisoning from leg casts of a synthetic plaster substitute. J. Am. Med. Assoc. 130:1222-1223.

Fitzpatrick, L.J. and Claire, D'D.C. (1947). Acute acetone poison

Pomerantz, R.B. (1950). Acute acetone poisoning from Castex. Am. J. Surg. 80:117-118.

Anon. (1952). Acetone poisoning and immobilizing casts. Br. Med. J. 2:1058.

Harris, L.C. and Jackson, R.H. (1952). Acute acetone poisoning caused by setting fluid for immobilizing casts. Br. Med. J. 2:1024-1026.

Renshaw, P.K. and Mitchell, R.M. (1956). Acetone poisoning following the application of a lightweight cast.

Br. Med. J. 1:615.

Hift, W. and Patel, P.L. (1961). Acute acetone poisoning due to a synthetic plaster cast. S. Afr. Med. J. 35:246-250.

Remark

Acetonemia and acetonuria have repeatedly been shown to be a clinical consequence of acute isopropanol (IPA) intoxication in humans. Most cases of IPA intoxication appear to involve the direct ingestion of a 70% solution by chronic alcoholics seeking a substitute for ethanol. Ketosis, narcosis, and gastric irritation are the most noteworthy observations following a severe IPA over-dose. Since IPA is rapidly and extensively metabolized to acetone, elevations in blood, urine, and breath acetone invariably accompany an isopropanol exposure. The acetone blood levels observed following a severe IPA overdose are generally very high and the time course for elimination from the blood is substantially longer than for the parent alcohol. Consequently, clinicians often detect acetone in the blood and urine of intoxicated patients long after IPA has disappeared from the body. The relatively slow elimination of acetone from the body is caused by saturation of the metabolic processes that control the rate of removed from tissues and organs. The tendency of the acetone blood levels to remain high and slowly return to normal control levels has hindered any reliable determination of a blood half-life.

Reference

Agarwal, S.K. (1979). Non-acidotic acetonemia: A syndrome due to isopropyl alcohol intoxication. J. Am. Med. Soc. NJ 76:914-916.

Hawley, P.C. and Falko, J.M. (1982). "Pseudo" renal failure after isopropyl alcohol intoxication. S. Med. J. 75:630-631.

Rosansky, S.J. (1982). Isopropyl alcohol poisoning treated with hemodialysis: Kinetics of isopropyl alcohol and acetone removal. J. Toxicol. Clin. Toxicol. 19:265-271.

Adelson, L. (1962). Fatal intoxication with isopropyl alcohol (rubbing alcohol). Am. J. Clin. Pathol. 38:144-151.

Brugnone, F., Perbellini, L., Apostoli, P., Bellomi, M., and

Caretta, D. (1983). Isopropanol exposure: Environmental and biological monitoring in a printing works. Br. J. Ind. Med. 40:160-168.

Triebig, G., Fritz, M., Schaller, K.H., Helbing, F., Bünte, E.M., Kufner, G., and Weltle, D. (1989). Arbeitsmedizinische Untersuchungen bei beruflich Iso-Propanol-exponierten Frauen. Arbeitsmed. Sozialmed. Praventivmed. 24:27-31.

Daniel, D.R., McAnalley, B.H., and Garriott, J.C. (1981). Isopropyl alcohol metabolism after acute intoxication in humans. J. Anal. Toxicol. 5:110-112.

Natowicz, M., Donahue, J., Gorman, L., Kane, M., McKissick, J., and Shaw, L. (1985). Pharmacokinetic analysis of a case of isopropanol intoxication. Clin. Chem. 31:326-328.

Lacouture, P.G., Heldreth, D.D., Shannon, M., and Lovejoy, F.H. (1989). The generation of acetonemia/ acetonuria following ingestion of a subtoxic dose of isopropyl alcohol. Am. J. Emerg. Med.7:38-40.

Pappas, A.A., Ackerman, B.H., Olsen, K.M., and Taylor, E.H. (1991). Isopropanol ingestion: A report of six episodes with isopropanol and acetone serum concentration time data. Clin. Toxicol. 29:11-21.

Monaghan, M.S., Olsen, K.M., Ackerman, B.H., Fuller, G.L., Porter, W.H., and Pappas, A.A. (1995). Measurement of serum isopropanol and acetone metabolite by proton nuclear magnetic resonance: Application to pharmacokinetic evaluation in a simulated overdose model. J. Toxicol. Clin. Toxicol. 33:141-149.

Remark

Several reports showing unusually high IPA blood levels in human post-mortem tissue specimens indicate that acetone can be reduced by aldehyde dehydrogenase to form IPA in situ. Blood levels of IPA ranging up to 0.44 g/L have been found in autopsy specimens from humans dying of liver disease, cardiovascular disease, or diabetes. High levels of IPA have also been seen in blood, liver, kidney, and brain

post-mortem specimens from individuals where the deaths were not related to IPA exposure. The highest IPA levels were generally found in the liver specimens (7-59 mg/dL) and the lowest in the brain (2-12 mg/dL).

Reference

Lewis, G.D., Laufman, A.K., McAnalley, B.H., and Garriott, J.C. (1984). Metabolism of acetone to isopropyl alcohol in rats and humans. J. Forensic Sci. 29:541-549.

Davis, P.L., Dal Cortivo, L.A., and Maturo, J. (1984). Endogenous isopropanol: Forensic and biochemical implications. J. Anal. Toxicol. 8:209-212.

Tiess, D. and Hammer, U. (1985). Über endogene Aceton-(Propan-2-on-)-und Isopropanol-(Propan-2-ol-)-Konzentrationen im menschlichen Körper nach ketoacidotischen Zusatänden. Z. Gesamte Hyg. 31:527-529.

Remark

High concentrations of acetone can increase the fibrinolytic activity of human plasma. In vitro studies have shown that acetone concentrations of 15.7 mmol/L or greater can activate the proteolytic and amidolytic enzymes necessary to dissolve polymerized fibrin. (This blood concentration would not be found following an 8 h occupational exposure to acetone.

Reference

Adamus, K. and Pajdak, W. (1994). Enhancement of fibrinolytic activity of human plasma in the presence of acetone. Scand. J. Clin. Lab. Invest. 54:353-359.

Adamus, K. and Pajdak, W. (1992). Amidolytic activities in acetone-treated human plasma. Folia Histochem. Cytobiolog. 30:219-222.

Hoem, N.-O. and Briseid, K. (1986). Activation of factor XII in acetone-treated human plasma: Significance of the functional state of plasma kallikrein for the extent of activation. Acta Pharmacol. Toxicol. 59:144-150.

Remark

The 1993 yearly summary of the American Association of Poison Control Centers listed 1062 incidents of human acetone poisoning throughout the United States. About 34% of the cases involved children less than six years old, and approximately 36% of cases required treatment in a

health care facility. No fatalities were reported in any of these incidents and there were seven major events. Cases involving exposure to the acetone in nail polish removers were reported in separate set of statistics that did not differ substantially from those involving pure acetone.

Reference — Litovitz, T.L., Clark, L.R., and Soloway, R.A. (1994). 1993 Annual report of the American Association of Poison Control Centers toxic exposure surveillance system. Am. J. Emerg. Med. 12:546-584.

Remark — Acetone has been used with no apparent difficulty to remove polymerized cyanoacrylate adhesives from the eyelid after three cases of accidental fusion.

Reference — Mindlin, A.M. (1977). Acetone used as a solvent in accidental tarsorrhaphy. Am. J. Ophthalmol. 83:136-137.

Remark — Acetone has found use as a pharmacological agent to treat actinic keratosis, to surgically correct palatal flaps in the mouth, to dissolve styrofoam ear impactions, to stop the vaginal hemorrhage from gynecological cancer, and to prevent the adverse effects of bleaching on tooth enamel.

Reference — Honigmann, K. (1994). The celluloid-acetone-dressing in palatoplasty. Cleft Palate Craniofac. J. 31:228-229.

White, S.J. and Broner, S. (1994). The use of acetone to dissolve a styrofoam impaction of the ear. Ann. Emerg. Med. 23:580-582.

Peikert, J.M., Krywonis, N.A., Rest, E.B., and Zachary, C.B. (1994). The efficacy of various degreasing agents used in trichloroacetic acid peels. J. Dermatol. Surg. Oncol. 20:724-728.

Pastner, B. (1993). Topical acetone for control of life threatening vaginal hemorrhage from recurrent gynecologic cancer. Eur. J. Gynacol. Oncol. 14:33-35.

Barghi, N. and Godwin, J.M. (1995). Reducing the adverse effect of bleaching on composite-enamel bond. J. Esthet. Dent. 6:157-161.

Remark — A woman being treated for alopecia areata became sensitized to the acetone used as a carrier to dissolve the

therapeutic agent. After handling acetone at work the patient developed acute contact dermatitis.

Reference: Tosti, A., Bardazzi, F., and Ghetti, P. (1988). Unusual complication of sensitizing therapy for alopecia areata. Contact Dermatitis 18:322.

Remark: Acetone did not cause any allergic skin reactions in skin prick tests with 136 volunteers. Acetone was used as a carrier at concentrations of 1% and 5% to test the allergic potential of low molecular weight acid anhydrides. No erythema or other allergic reactions were noted in the vehicle controls.

Reference: Drexler, H., Schaller, K.-H., Weber, A., Letzel, S., and Lehnert, G. (1993). Skin prick tests with solutions of acid anhydrides in acetone. Int. Arch. Allergy Immunol. 100:251-255.

Remark: Acute subjective complaints and states of well-being were assessed in a group of employees exposed to acetone in a cellulose acetate plant. The study was performed on three consecutive days during the summer when temperatures within the facility were 40°C (104°F) or higher. The mean 4-h TWA exposure concentration of acetone was approximately 940 ppm with individual TWAs ranging from 475 to 1500 ppm. When the results from the first questionnaire, a 17-item subject symptom survey, were arbitrarily divided into four complaint categories, two categories (discomfort and irritation) appeared to dominate the severity scores and showed a correlation with the total amount of acetone excreted in the urine over the 8-h shift. The total score for all complaints did not, however, correlate with the exposure concentration. The results from a second questionnaire on well-being indicated that annoyance was the only complaint that correlated with the ambient airborne concentration of acetone. Scores for all four of the well-being categories correlated with the total 8-hr urine acetone value.

Reference: Kiesswetter, E., Blaszkewicz, M., Vangala, R.R., and Seeber, A. (1994). Acute exposure to acetone in a factory and ratings of well-being. Neurotoxicology 15:597-602.

Seeber, A., Blaszkewicz, M., Golka, K. Kiesswetter, E., Vangala, R.R., and Bolt, H.M. (1993). Exposure to acetone

and neurobehavioral effects: Comparisons of two experiments and a field study. In: Proceedings 24th International Congress on Occupational Health, Nizza, Italy.

Seeber, A., Blaszkewicz, M., Kiesswetter, E., and Vangala, R.R. (1993). Untersuchungs-bericht zum Einflu von Aceton auf das Befinden von Schichtmitarbeitern im Werk Frieberg der Rhone-Poulenc Rhodia AG. Institute of Occupational Health, University of Dortmund, Dortmund, Germany.

Remark

Acute subjective complaints and states of well-being were measured in a group of 16 male students exposed to acetone under laboratory conditions. The subjects received either a 1000 ppm acetone exposure, a com-bined exposure to 500 ppm acetone and 200 ppm ethyl acetate, or an exposure to filtered room air. Data were collected using two questionnaires, a 17-item subject symptom survey and a 4-item well-being questionnaire. An increase in irritative complaints was noted during the acetone exposures; however, reports of discomfort, tired-ness, and difficulties in breathing were not affected. Responses on the complaints and annoyance scales from the well-being questionnaire also increased during the exposures; but the increases did not correlate the urinary excretion of acetone. The odor of acetone may have influenced the subjective symptom ratings.

Reference

Seeber, A. and Kiesswetter, E. (1991). Exposure to mixtures of organic solvents: Subjective symptoms as valid adverse effects? In: Proceedings of the 4th International Conference on the Combined Effects of Environmental Factors, L.D. Fechter, ed., pp. 71-74.

Seeber, A., Kiesswetter, E., Vangala, R.R., Blaszkewicz, M., and Golka, K. (1992). Combined exposure to organic solvents: An experimental approach using acetone and ethyl acetate. Appl. Psychol.: Int.Rev. 41:281-292.

Seeber, A., Kiesswetter, E., and Blaszkewicz, M. (1992). Correlations between subjective disturbances due to acute exposure to organic solvents and internal dose. Neurotoxicology 13:265-270.

Remark

A group of about 20 male and female volunteers were exposed to either 250 ppm of acetone or to a combin-ation of 125 ppm of acetone and 200 ppm of methyl ethyl ketone (MEK) for 4 h. Four psychomotor tests, one sensorimotor test, and one psychological test were performed on the subjects before, during, and after the exposure session. Acetone was shown to cause an effect on the responses obtained in two of these tests, a dual auditory tone discrimination compensatory tracking test and a profile of mood states (POMS) test. Relative to preexposure control values, the 250 ppm acetone exposure caused an increase in both the response time and the percentage of incorrect responses in the auditory tone portion of the dual task when the tests were pre-sented in series. The response measurements were not affected by the exposure when both portions of the dual task were presented simultaneously. Statistically different results were only obtained during the first 2-h exposure session and during the 2-h post-exposure session. Male subjects taking the POMS test showed an increase in the anger-hostility portion of the test. The effects were noted to be very subtle and the authors were cautious in their evaluation and interpretation of the abnormal results.

Reference

Dick, R.B., Brown, W.D., Setzer, J.V., Taylor, B.J., and Shukla, R. (1988). Effects of short duration exposures to acetone and methyl ethyl ketone. Toxicol. Lett. 43:31-49.

Dick, R.B., Setzer, J.V., Taylor, B.J., and Shukla, R. (1989). Neurobehavioral effects of short duration exposures to acetone and methyl ethyl ketone. Br. J. Ind. Med. 46:111-121.

Brown, W.D., Setzer, J.V., Dick, R.B., Phipps, F.C., and Lowry, L.K. (1987). Body burden profiles of single and mixed solvent exposures. J. Occup. Med. 29:877-883.

Remark

Reaction times were measured in a group of six male university students who received six consecutive daily exposures to acetone vapors at concentrations of 250 and 500 ppm. The exposures lasted 6 h/day, with a 45-min lunch break separating the 3-h morning and afternoon segments. An additional 250 ppm (6 h/day) acetone

exposure was conducted in a group of subjects who exercised to double their metabolic rate. A neuro-physiology test measured the reaction time to a visual stimulus presented four times during each exposure session. The responses obtained during each exposure session varied considerably between individuals and were not statistically different from an untreated control group; however, when the data from each exposure day were averaged for all subjects and expressed relative to a preexposure control value, several statistically significant changes were obtained. The response times were longer on each of the six exposure days for the 500 ppm group, and two of the six exposure days for the both of the 250 ppm exposure groups.

Reference — Matsushita, T., Goshima, E., Miyakaki, H., Maeda, K., Takeuchi, Y., and Inoue, T. (1969). Experimental studies for determining the MAC value of acetone. 2. Biologic reactions in the "six-day exposure" to acetone. Jpn. J. Ind. Health 11:507-515.

Remark — Neurophysiological tests were performed on groups of eight or nine male volunteers exposed to acetone at concentrations of 250 to 270 ppm or 500 to 750 ppm for two 3-h sessions with a 1-h break. Spontaneous and evoked changes in five physiological functions were recorded before, during, and at the end of the exposure, but only those data collected at the end of the experiment were compared with control values due to wide varia-tions in the baseline values. The following non-statistical tendencies were noted for the exposed groups: a decrease in the spontaneous galvanic skin response; a decrease in evoked vasoconstriction activity; a decrease in the mean length of time for ten heart beats; and an increase in cerebral activity. An increase in air temperature within the exposure chamber was found to be positively cor-related with several of the adverse responses.

Reference — Suzuki, H. (1973). An experimental study on physio-logical functions of the autonomic nervous system of man exposed to acetone gas. Jpn. J. Ind. Health 15:147-164.

Remark — Time estimation tests were performed on two male and two female student volunteers exposed to acetone vapors for 4 h on a single day. The 4-hr exposure was com-posed of two

2-h sessions with a 2-h rest period sep-arating the sessions. The study was not conducted at a constant acetone exposure concentration because of difficulties controlling airflow in the chamber. Two exposure ranges were defined; a low level acetone exposure at vapor concentrations ranging between 170 and 450 ppm, and a high level exposure at concentrations ranging between 450 and 690 ppm. At 30 min intervals, the subjects were asked to estimate the passage of time for periods lasting from 5-30 sec. Relative to control values, the time estimations tended to be more prolonged for male and female subjects at both exposure concentration ranges.

Reference: Nakaaki, K. (1974). An experimental study on the effect of exposure to organic solvent vapor in human subjects. J. Sci. Labour 50:89-96.

Remark: Reaction time tests were conducted with a group five occupationally exposed employees working on a production line where acetone was used in a solvent- based glue. The workplace concentration of acetone was reported to be about 200 ppm. Reaction times were determined following presentation of a concurrent light and sound stimulus. Test results were obtained both before and after an 8-h work shift; control values were obtained on the same group of employees two days after being removed to an acetone-free work area. Highly variable results were obtained upon repeated testing. A statistically significant increase was observed in the reaction time when the mean values for each individual were averaged for the 5 subjects.

Reference: Israeli, R., Zoref, Y., Tessler, Z., and Braver, J. (1977). Reaktionszeit als Mittel zur Aceton-TLV-(MAK)-Wertbestimmung. Zbl. Arbeitsmed. 27:197-199.

Remark: The neurotoxic effects of repetitive acetone exposures were examined in groups of male and female volunteers. Two small groups of male subjects were exposed to vapor concentrations of 200, 1000, or 1250 ppm for either 3.0 hr or 7.5 h/day and 4 days/week. Following the fourth week of exposure at 1250 ppm of acetone, the two groups were given a fifth week at 0 ppm and then a final week where the vapor concentration was allowed to fluctuate between 750 and 1250 ppm (average of 1000 ppm). A battery of neurophysiological and neurobe-havioral tests were

performed at various times throughout the exposures. The neurophysiological tests included spontaneous electroencephalograms, visual evoked response using a strobe light, and a Romberg heel-to-toe equilibrium examination. Cognitive neurobehavioral testing included an arithmetic test, a coordination test, and a visual inspection test. Male subjects exposed to 1250 ppm of acetone for 7.5 h showed a statistically significant increase in the amplitude of the visual evoked response when compared to background values. This effect was not observed in male or female subjects exposed to 1000 ppm of acetone for 7.5 h/day.

Reference: Stewart, R.D., Hake, C.L., Wu, A., Graff, S.A. Forster, H.V., Keeler, W.H., Lebrun, A.J., Newton, P.E., and Soto, R.J. (1975). Acetone: Development of a biologic standard for the industrial worker by breath analysis. U.S. Dept. of Commerce, National Technical Information Service PB82-172917.

Remark: An average of ten male and female university students were exposed for 3 to 5 min in an exposure chamber and then asked to subjectively rate the degree of eye, nose, and throat irritation from the exposure. Slight irritation was experienced by some of the subjects exposed to 300 ppm of acetone, but most of the subjects reportedly tolerated 500 ppm without severe effect.

Reference: Nelson, K.W., Ege, Jr., J.F., Ross, M., Woodman, L.E., and Silverman, L. (1943). Sensory response to certain industrial solvent vapors. J. Ind. Hyg. Toxicol. 25:282-285.

Remark: Two groups of four volunteers exposed to either 200 or 500 ppm of acetone for 2 h did not experience any subjective symptoms of irritation other than an odor awareness at 500 ppm. Blood specimens collected before and after treatment showed no changes in hematological or biochemical values.

Reference: DiVincenzo, G.D., Yanno, F.J., and Astill, B.D. (1973). Exposure of man and dog to low concentrations of acetone vapor. Am. Ind. Hyg. Assoc. J. 34:329-336.

Remark: The local and systemic effects of repetitive acetone exposures were examined in groups of male and female volunteers studied under controlled conditions. Two groups of 2 to 4 male subjects were exposed to each of four

vapor concentrations (0, 200, 1000, and 1250 ppm) for either 3.0 h or 7.5 h/day for 4 days/week. Following the fourth week of exposure at 1250 ppm of acetone, the two groups were given a fifth week at 0 ppm and then a final week where the vapor concentration was allowed to fluctuate between 750 and 1250 ppm (average of 1000 ppm). A weekly medical exam included a complete blood count and a 23 element clinical chem-istry analysis. Blood pressure, temperature, subjective responses, clinical signs and symptoms, and urinalysis were recorded daily. Cardiopulmonary testing (heart rate, minute ventilation, expiratory flow rate, alveolar-capillary gas exchange, and vital capacity) was performed shortly before the end of each weekly exposure session. The acetone exposures were not found to produce any statistically significant changes in the clinical or physiological tests. A battery of neurophysio-logical and neurobehavioral tests were also performed at various times throughout the study. Except for one test, no neurotoxic effects were observed to result from the acetone exposures. Male subjects exposed to 1250 ppm of acetone for 7.5 h did, however, respond with a statistically significant increase in the amplitude of the visual evoked response test. Subjective complaints of eye irritation, throat irritation, headache, tiredness were noted at all of the exposure concentrations including the 0 ppm control level. Three of the four women in the group exposed to 1000 ppm of acetone for 7.5 h were noted to have begun their menstrual period earlier than normal.

Reference

Stewart, R.D., Hake, C.L., Wu, A., Graff, S.A. Forster, H.V., Keeler, W.H., Lebrun, A.J., Newton, P.E., and Soto, R.J. (1975). Acetone: Development of a biologic standard for the industrial worker by breath analysis. U.S. Dept. of Commerce, National Technical Information Service PB82-172917.

Remark

A single resting individual exposed to either 211 or 2110 ppm of acetone for 8 h was not found to experience any loss of judgment or coordination. Negative findings were also obtained in a group of subjects that exercised moderately the 2110 ppm exposure and in a group that was exposed for three days at 2110 ppm (8 h/day).

Reference

Haggard, H.W., Greenberg, L.A., and Turner, J.M. (1944). The physiological principles governing the action of

acetone together with the determination of toxicity. J. Ind. Hyg. Toxicol. 26:133-151.

Remark

A group of five male university students received a single exposure to acetone at concentrations of either 0, 100, 250, 500, or 1000 ppm for 6 h/day. Using a test questionnaire, up to seven different symptoms were subjectively ranked (0 to 2) and multiplied by the number of student complaints recorded (0 to 5). The seven symptoms of interest were: unpleasant odor, tension, headache, general weakness, lack of energy, heavy eyes, and mucous membrane irritation. The groups exposed to 500 and 1000 ppm responded with total scores of 4-5 for the first five interview sessions, whereas the groups exposed to 100 and 250 ppm had scores of 0-1. On the morning following the exposure, students in the 500 and 1000 ppm exposure groups had scores of 6-12 for the following four symptoms: tension, general weakness, heavy eyes, and lack of energy. For the 1000 ppm exposure, the average peak post-exposure blood and urine concentrations of acetone were about 60 and 53 mg/L respectively. Exposures at 500 or 1000 ppm resulted in a temporary decrease in the phagocytic activity of neutrophils and an increase in the eosinophil and leukocyte counts in peripheral blood specimens collected at 3, 7, 24, and 32 hr post-exposure.

Reference

Matsushita, T., Yoshimune, A., Inoue, T., Yamada, S., and Suzuki, H. (1969). Experimental studies for determining the MAC value of acetone. 1. Biologic reactions in the "one-day exposure" to acetone. Jpn. J. Ind. Health 11:477-485.

Remark

A group of six male university students received six consecutive daily exposures to acetone vapor at concentrations of either 250 or 500 ppm for 6 h/day. Using the same test questionnaire described above, up to seven different symptoms were subjectively ranked (0 to 2) and multiplied by the number of student complaints recorded (0 to 6). For the 500 ppm exposure, mucous membrane irritation was reported to be greatest immediately after entering the chamber in the morning and the afternoon exposure sessions. Appreciable accommodation was noted as each exposure continued, but no day-to-day adaptation was observed. Irritation to the throat was much less severe

than to the eyes and nose. Complaints recorded on the day after each exposure were similar to those described for the single day treatment. Hemato-logical abnormalities were detected in blood specimens from the 500 ppm-exposed subjects that were similar to those found in subjects exposed for a single day.

Reference: Matsushita, T., Goshima, E., Miyakaki, H., Maeda, K., Takeuchi, Y., and Inoue, T. (1969). Experimental studies for determining the MAC value of acetone. 2. Biologic reactions in the "six-day exposure" to acetone. Jpn. J. Ind. Health 11:507-515.

Remark: Nine press operators in a cellulose acetate production plant were monitored for signs and symptoms of sensory irritation during and after multiple 8-h workshifts. Breathing zone samples produced an average 8-h time-weighted average exposure of 1006 ppm (950 to 1060 ppm range) for one 7-day survey period. Indi-vidual breathing zone samples ranged as high as 5500 ppm when the filters were removed from the presses. Subjects were asked to report and rate (slight, mild, or strong) any symptoms of sensory irritation following each sample collection. Reports of irritation were as follows: eye irritation in 7, throat irritation in 4, headache and lightheadedness in 3, and nasal irritation in 2 employees. The symptoms were transient and generally occurred when the vapor concentrations exceeded 1000 ppm. Of the 31 individual reports of eye irritation, 21 occurred when the acetone concentration was greater than 1500 ppm; only four slight to mild responses were obtained when the instantaneous concentration was between about 750 and 1000 ppm. Medical exams performed at the end of each workshift were essentially normal in all respects except for slight redness in the nasal mucosa of one individual and slight congestion in the nose and throat of another.

Reference: Raleigh, R.L. and McGee, W.A. (1972). Effects of short, high-concentration exposures to acetone as determined by observation in the work area. J. Occup. Med. 14:607-610.

Remark: Two human volunteers took ten breaths of acetone vapor of a known concentration to determine the irritancy potential of acetone. The first individual inhaled 6000 ppm of acetone and did not experience any throat irritation;

however, the subject did experience nausea, suffocation, and slight dizziness as a result of the exposure. The second volunteer was exposed to 8000 ppm of acetone and felt nausea, a mild anesthetic feeling, and peripheral vasodilatation. The second subject also failed to feel any throat irritation and the plethysmo-graphic results showed little change in ether airway resistance or thoracic gas volume. In subsequent experiments each subject was exposed to increasing concentrations of acetone vapor that was delivered to the eyes through tight fitting goggles. At the end of a 15 sec exposure period, neither subject reported any irritant effects at a vapor concentration of 1000 ppm. When the concentration was increased to 2000 ppm, one subjected reported lacrimation and the other reported a stinging sensation immediately after opening the eyes. Increasing the concentration to 4000 ppm caused both subjects to experience a brief stinging sensation that disappeared after 5-10 sec. At 10,000 ppm of acetone, the subjects reported lacrimation but no strong irritancy.

Reference

Douglas, R.B. and Coe, J.E. (1987). The relative sensitivity of the human eye and lung to irritant gases. Ann. Occup. Hyg. 31:265-267.

Douglas, R.B. (1981). Inhalation of irritant gases and aerosols. In: International Encyclopedia of Pharmacology and Therapeutics, Vol. 104, Chapter 15, pp. 297-333.

Remark

Humans have been shown to be very sensitive to the odor of acetone with the olfactory nerve capable of detecting slight changes in the airborne vapor concen-tration. Using psychophysical techniques, the slope of the odor intensity versus concentration curve for acetone vapor has been tested repeatedly and shown to range from 0.54 to 0.71 in human volunteers exposed briefly to acetone concentrations of about 100-240,000 ppm (0.05% to 100% of airborne saturation).

Reference

Moncrief, R.W. (1957). Olfactory adaptation and odor intensity. Am. J. Psychol. 70:1-20.

Cain, W.S. (1969). Odor intensity: Differences in the exponent of the psychophysical function. Percept. Psychophys. 6:349-354.

Berglund, B., Berglund, U., Ekman, G., and Engen, T. (1971). Individual psycho-physical functions for 28 odorants. Percept. Psychophys. 9:379-384.

Berglund, B. and Olsson, M.J. (1993). Odor-intensity interaction in binary and ternary mixtures. Percept. Psychophys. 53:475-482.

Remark

Differences in the perceptual response caused by the odor and irritancy effects of acetone and 46 other chemicals have been determined by measuring the relative response intensity in three types of subjects: anosmic subjects who lacked any sense of smell, normal subjects trained to respond only to trigeminal nerve stimulation, and normal subjects who responded to both trigeminal and olfactory nerve stimulation. Each group consisted of 15 volunteers who were asked to rank the relative intensity of a 5 sec exposure to the concentrated vapors. All of the individuals in each test group were able to detect the vapors of acetone and each of three test groups gave acetone a high intensity ranking, which indicated that acetone could cause a high degree of irritation and odor awareness when tested at the vapor pressure limit (ca. 240,000 ppm).

Reference

Doty, R.L. (1975). Intranasal trigeminal detection of chemical vapors by humans. Physiol. Behav. 14:855-859.

Doty, R.L., Brugger, W.L., Jurs, P.C., Orndorff, M.A., Snyder, P.J., and Lowry, L.D. (1978). Intranasal trigeminal stimulation from odorous volatiles: Psychometric responses from anosmic and normal humans. Physiol. Behav. 20:175-185.

Remark

The odor and irritancy thresholds for acetone were assessed in a group of four anosmic and normosmic volunteers. The vapors were self administered from the head space of squeeze bottles that contained graded dilutions of acetone in water. Acetone vapors were found to have an irritancy threshold of approximately 100,000 ppm under these conditions. Below the irritancy threshold concentration, the anosmic subjects were unable to detect the presence of acetone vapors. The odor threshold for acetone vapors was determined to be about 10,000 ppm.

Reference

Cometto-Muñiz, J.E. and Cain, W.S. (1994). Perception of

odor and nasal pungency from homologous series of volatile organic compounds. Indoor Air 4:140-145.

Cometto-Muñiz, J.E. and Cain, W.S. (1993). Efficacy of volatile organic compounds in evoking nasal pungency and odor. Arch. Environ. Health 48:309-314.

Remark

The frequency distribution of odor threshold data was examined in 970 male and female subjects. A bimodal distribution was obtained for the odor threshold concentration of acetone which suggested that a genetic polymorphism may exist for odor sensitivity to acetone vapors. Approximately 10% of the subjects were found to have a high odor sensitivity to acetone and could detect the vapors in the headspace from aqueous concentrations of 0.25% or less.

Reference

Odeigah, P.G.C. (1994). Smell acuity for acetone and its relationship to taste ability to phenylthiocarbamide in a Nigerian population. E. Afr. Med. J. 71:462-466.

Remark

The mortality rates and clinical laboratory results were examined for 948 employees exposed to acetone for up to 23 years while producing cellulose acetate fiber. The workers were divided into three groups and used as controls in a larger epidemiology study focusing on methylene chloride. The median 8-h time-weighted-average acetone exposure concentrations were 380, 770, and 1070 ppm. No statistical differences were found for either the men or the women in the acetone-exposed groups when compared to the US general population. The total death rates from all causes, cardiovascular disease, and total malignant neoplasms were below expectation by 55%, 61%, and 43%, respectively. There was no indication that occupational acetone exposures up to 1070 ppm had an adverse affect on selected hematologic and clinical chemistry determinations.

Reference

Ott, M.G., Skory, L.K., Holder, B.B., Bronson, J.M., and Williams, P.R. (1983). Health evaluation of employees occupationally exposed to methylene chloride. General study design and environmental considerations. Scand. J. Work Environ. Health 9(Suppl.1):1-7.

Ott, M.G., Skory, L.K., Holder, B.B., Bronson, J.M., and Williams, P.R. (1983). Health evaluation of employees

occupationally exposed to methylene chloride. Mortality. Scand. J. Work Environ. Health 9(Suppl.1):8-16.

Ott, M.G., Skory, L.K., Holder, B.B., Bronson, J.M., and Williams, P.R. (1983). Health evaluation of employees occupationally exposed to methylene chloride. Clinical laboratory evaluation. Scand. J. Work Environ.Health 9(Suppl.1):17-25.

Remark

A group of 60 volunteers employed for at least five years in an acetate fiber manufacturing facility were divided into two equal groups according to their level of acetone exposure. The high exposure group had personal TWA exposures ranging from 948-1048 ppm and the low exposure group had exposures ranging from 549-653 ppm. The two test groups were compared to a single group of 60 controls that had never been exposed to acetone. Blood specimens from each of the subjects were analyzed for changes in glucose, glutamic pyruvic transaminase, glutamic oxaloacetic transaminase, γ-glutamyl transpeptidase, protein electrophoresis patterns, blood urea nitrogen, creatinine, platelet count, and red and white blood cell counts. After taking into consideration risk factors, past medical histories, and age, no statistically significant differences were noted between the test groups and the controls.

Reference

Grampella, D., Catenacci, G., Garavaglia, L., and Tringali, S. (1987). Health surveillance in workers exposed to acetone. In: Proceedings of the VII International Symposium on Occupational Health in the Production of Artificial Organic Fibres, pp. 137-141. Wolfheze, Holland.

Remark

Medical surveillance of approximately 100 employees co-exposed to methylene chloride and acetone in an acetate fiber plant has failed to show any evidence of acetone-induced potentiation of methylene chloride hepato-toxicity. The 8-hr TWA exposure concentrations to acetone and methylene chloride were 900 ppm and 475 ppm, respectively. Blood SGOT(AST), SGPT(ALT), bilirubin, and hematocrit levels in the exposed group were not statistically different from an unexposed control group.

Reference

Soden, K.J. (1993). An evaluation of chronic methylene chloride exposure. J. Occup. Med. 35:282-286.

Remark	An occupational health survey was conducted for two days on 110 male workers exposed to TWA acetone concentrations ranging from 5 to 1212 ppm (average value 350 ppm) for an mean of 14.9 years. The employees worked in three factories that produced cellulose acetate fibers. They were divided into the following three categories groups according to their level of exposure: low (less than 250 ppm); medium (250 to 500 ppm); and high (greater than 500 ppm). A large subjective symptom questionnaire was administered to each employee that solicited information on symptoms experience before and after work and during the last 6 month period. Five neurobehavioral test were also performed along with tests of autonomic nervous system function, liver function, phagocytic function, and hema-tology. Concentration related changes were noted in several of the responses from the questionnaires, including eye inflammation and irritation, loss of weight, faint or heavy feeling in the head, and nausea. The neurobehavioral tests, clinical chemistry measurements, and hematology results did not show any clear exposure response relationship relative to an unexposed control population.
Reference	Satoh, T., Omae, K., Nakashima, H., Takebayashi, T., and Sakurai, H. (1994). Cross-sectional study of effects of acetone exposure on workers' health. In: Proceedings of the 9th International Symposium in Epidemiology in Occupational Health, pp. 407-412. Cincinnati, OH. Sakurai, H. (1994). Epidemiology as a tool for occupational standard setting. In: Proceedings of the 9th International Symposium in Epidemiology in Occupational Health, pp. 67-84. Cincinnati, OH.
Remark	Information from medical department visits, lost-time records, and comprehensive medical examinations were summarized for thousands of workers with up to 18 years of industrial exposure to acetone in a cellulose acetate production facility. After compiling and reviewing over 21 million man-hours of acetone exposure, the authors found no difference in the incidence of illness relative to appropriate control populations. Mild transient symptoms of irritation were recorded when the average exposure

concentrations exceeded 2500 ppm. The authors concluded that, based on years of employee experience, acetone concentrations up to 1500 ppm would be without injurious or objectionable effects for a continuous exposure of up to 8 hr.

Reference: Oglesby, F.L., Williams, J.L., and Fassett, D.W. (1949). Eighteen-year experience with acetone. Presentation from the Annual Meeting of the American Industrial Hygiene Association. Detroit, Michigan.

Remark: A clinical evaluation was performed on 45 men and 39 women employed in an assembly operation where acetone was used as a solvent. Blood specimens from the employees were used to determine the hemoglobin concentration, coagulation time, sedimentation rate, red and white blood cell counts, and white blood cell differ-ential counts. The clinical measurements revealed a below normal hemoglobin concentration in several of the women, which was attributed to their poor nutritional status. The authors concluded that the acetone exposures did not cause any hematological abnormalities.

Reference: Rösgen and Mamier (1944). Sind Azetongase blutschä-digend? Öffentl. Gefundheitsdienft 10:A83-A86.

Remark: The nasal retention of acetone vapors was examined in two human volunteers who inhaled concentrations of 126 and 1264 ppm (300 and 3000 mg/m^3). The nasal reten-tion of acetone was independent of the vapor concentra-tion and varied between 18 and 40% of the inhaled con-centration when inhaled through the nose and out the mouth at a flow rate of 18 L/min. The lung retention of acetone vapors was determined following the inspiration of a controlled volume of air containing a vapor concen-tration of 337 and 4635 ppm (800 and 11,000 mg/m^3). The lung retention ranged from 53-61% of the inhaled concentration and was independent of either the acetone vapor concentration, the length of time the breath was held, or the volume of air exhaled.

Reference: Landahl, H.D. and Hermann, R.G. (1950). Retention of vapors and gases in the human nose and lung. Arch. Ind. Hyg. 1:36-45.

Remark: The percentage of acetone absorbed from the smoke of two

non-filter cigarettes containing 0.56 mg of acetone per 35 mL puff of smoke was assessed using 16 male and female subjects. The average retention of acetone was 56% for the mouth and 86% for the lung.

Reference

Dalhamn, T., Edfors, M-L., and Rylander, R. (1968). Mouth absorption of various compounds in cigarette smoke. Arch. Environ. Health 16:831-835.

Dalhamn, T., Edfors, M-L., and Rylander, R. (1968). Retention of cigarette smoke components in human lungs. Arch. Environ. Health 17:746-748.

Remark

The respiratory retention, alveolar uptake, and alveolar excretion of acetone was determined in five male and five female subjects exposed to about 130 ppm of acetone for 4 h. The retention of acetone was found to decline during the first 2 h of exposure and then plateau with a mean value varying between 11 and 18%. A statistically significant sex difference was observed for body reten-tion and alveolar uptake with men displaying higher percentages than women. The respiratory excretion data were described by a two-compartment pharmacokinetic model for the men and a one-compartment model for the women. The rate of respiratory excretion was very slow with smaller amounts of the absorbed acetone expired by women than by men.

Reference

Nomiyama, K. and Nomiyama, H. (1974). Respiratory retention, uptake and excretion of organic solvents in man. Benzene, toluene, n-hexane, trichloroethylene, acetone, ethyl acetate and ethyl alcohol. Int. Arch. Arbeitsmed. 32:75-83.

Nomiyama, K. and Nomiyama, H. (1974). Respiratory elimination of organic solvents in man. Benzene, toluene, n-hexane, trichloroethylene, acetone, ethyl acetate and ethyl alcohol. Int. Arch. Arbeitsmed. 32:85-91.

Remark

Two subjects inspired 20,000 ppm of acetone in a single breath and forcibly exhaled after holding their breath for a period of time ranging from 1.5 to 15 sec. The acetone concentration in the air at the beginning and end of the breath-holding period provided a measurement of the acetone removed by the capillary blood flowing to the lung. When the theoretical and actual values were compared, the

rate of acetone removal by the lung was found to be about 8 times slower than predicted. A substantial portion of the inhaled acetone was believed to have adsorbed into the pulmonary tissue upon inspiration and then desorbed during expiration, thus contaminating the expired alveolar air sample used for analysis.

Reference: Cander, L. and Forster, R.E. (1959). Determination of pulmonary parenchymal volume and pulmonary capillary blood flow in man. J. Appl. Physiol. 59:541-551.

Remark: The uptake of acetone was determined in 33 male and female volunteers who inhaled 1 to 3 breaths of air that contained 180 to 690 ppm of acetone vapor. The acetone was inhaled with either ordinary or deep respirations. The uptake of acetone was found to range between 65% and 85% for the male and female subjects. A higher percentage of acetone was absorbed with deep respirations than with ordinary breaths.

Reference: Teramoto, K., Horiguchi, S., Nakaseko, H., and Kageyama, M. (1987). Initial uptake of organic solvents in the human body by short-term exposure. J. Sci. Labour 63:13-19.

Remark: Data from male subjects showed that inhaled acetone is partially desorbed from the fluid and tissues lining the respiratory tract during exhalation. Subjects were tested at rest and at progressively increasing work loads using inspired acetone concentrations of 0.01% (100 ppm) and 0.1% (1000 ppm). The wash-in/wash-out behavior was ascribed to the initial absorption of acetone into the non-perfused tissues lining the upper airways (i.e., the nose, pharynx, and bronchi) during the wash-in period. The extent of dissolution and re-entrainment of acetone vapors was affected by the volume of dead space air in the lung (i.e., the rate of ventilation).

Reference: Schrikker, A.C.M., de Vries, W.R., Zwart, A., and Luijendijk, S.C.M. (1989). The excretion of highly soluble gases by the lung in man. Pflügers Arch. Eur. J. Physiol. 415:214-219.

Schrikker, A.C.M., de Vries, W.R., Zwart, A., and Luijendijk, S.C

Remark: Five male subjects were exposed on four different occasions to about 84 ppm (200 mg/m^3) of acetone vapor

for 2 h. The subjects were tested either at rest or while exercising on a bicycle ergometer at a rate of 25, 50, or 75 watts. The percentage of acetone retained by the body remained relatively constant at 40-44% of the inhaled concentration as the pulmonary ventilation increased with higher work loads. The rate of acetone uptake by the body was determined to be directly proportional to the ventilation rate.

Reference: Jakubowski, M. and Wieczorek, H. (1988). The effects of physical effort on pulmonary uptake of selected organic compound vapours. Pol. J. Occup. Med. 1:62-71.

Remark: Fasting was found to affect the absorption rate of acetone when a 137 mg/kg dose of acetone was consumed. On an empty stomach, the blood levels of acetone rose rapidly and a peak blood level of 310 mg/g was observed at 10-min post-treatment. In contrast, the absorption was much slower after a meal with a peak blood level of 190 mg/g at 42 min post-ingestion.

Reference: Widmark, E.M.P. (1919). Studies in the concentration of indifferent narcotics in blood and tissues. Acta Med. Scand. 52:87-164.

Remark: Acetone was found to be excreted through the skin, into the saliva, and into exhaled air following the ingestion of a 80 mg/kg oral dose by a single subject. Acetone was detected in duodenal juice following the intravenous administration of a 40 mg/kg dose; the venous acetone blood level was 72.5 mg/L. Application of 15 g of acetone onto the exposed skin of single individual over a 30 min period resulted in an acetone blood level of 40 mg/L, a urine level of 70 mg/L, and an expired air concentration of 107 g/L.

Reference: Parmeggiani, L. and Sassi, C. (1954). Occupational poisoning with acetone - Clinical disturbances, investigations in workrooms and physiopathological research. Med. Lav. 45:431-468.

Remark: The blood clearance of acetone was investigated using diabetic and healthy individuals administered a 10 g (ca. 140 mg/kg) dose by iv infusion over a 2-h period. The average peak blood level of acetone at the end of the infusion was found to be 230 mg/L in the healthy subjects and 195 mg/L in the diabetic patients. The elimination of

acetone from the blood was noted to be extremely slow for both groups with the rate of decline being somewhat faster in the diabetic patients. The initially slow disappearance of acetone from the blood was thought to be due to the saturation of acetone metabolism.

Reference: Koehler, A.E., Windsor, E., and Hill, E. (1941). Acetone and acetoacetic acid studies in man. J. Biol. Chem. 140:811-825.

Remark: Blood levels were measured in a middle-aged painter who was estimated to have consumed about 600 mL of paint thinner that contained a large amount of acetone. Unknown amounts of methanol and ethanol were also consumed before admission to a hospital about 26 h after the event. The patient's blood acetone level was found to be 2.0 mg/L two days after the event, and the breath acetone content was calculated to be 21 mg/L at the time of admission.

Reference: Rooth, G. and Östenson, S. (1966). Acetone in alveolar air, and the control of diabetes. Lancet II:1102-1105.

Remark: The pharmacokinetics of acetone was estimated in subjects given oral dosages ranging from 40-70 mg/kg. The percentage of absorbed acetone eliminated by excretion was found to decrease as the blood levels declined, ranging from a high of 36% to a low of 7%. The percentage of ingested acetone undergoing metabolism was calculated to increase from 64-94% as the blood levels fell from 73 to 2 mg/L. Periodic estimations of the metabolism rate for acetone showed a decrease from about 2.1-1.1 mg/kg/h over a 24-h period, indicating that the metabolic rate was related to the amount of acetone in the blood (i.e., the rate was apparently first-order). The rate of acetone metabolism before and during exercise increased from about 2.7 to 6.0 mg/kg/h.

Reference: Haggard, H.W., Greenberg, L.A., and Turner, J.M. (1944). The physiological principles governing the action of acetone together with the determination of toxicity. J. Ind. Hyg. Toxicol. 26:133-151.

Remark: The kinetics of acetone was examined in resting and exercising male volunteers exposed for 8 h to 422, 1266, and 2110 ppm (1, 3, and 5 mg/L) of acetone. The end-

exposure blood concentrations of acetone were found to be 30, 99, and 165 mg/L for the 422, 1266, and 2110 ppm exposures, respectively. A two-fold increase in the acetone blood level and a 3-fold increase in the ventilation rate occurred when a subject was exposed to 422 ppm with moderate physical exercise. End-exposure blood levels of acetone in an individual exposed to 2110 ppm of acetone for three consecutive days were 162, 180, and 182 mg/L for the first, second, and third day. The blood level obtained 2 h after the start of the last exposure was 91 mg/L. The highest concentrations of acetone not causing any day-to-day accumulation within the body were estimated to be 1266 ppm for a resting individual and 422 ppm for a moderately active person.

Reference — Haggard, H.W., Greenberg, L.A., and Turner, J.M. (1944). The physiological principles governing the action of acetone together with the determination of toxicity. J. Ind. Hyg. Toxicol. 26:133-151.

Remark — Healthy male subjects were exposed for 2 h to acetone vapor concentrations of 552, 300, or 311 ppm and physiological variables such as heart rate, oxygen uptake, and pulmonary ventilation were recorded along with the venous and arterial blood levels of acetone. The uptake of acetone was found to remain relatively constant at about 43% of the exposure concentration, regardless of the exposure regimen involved. The blood acetone concentration increased continuously during exposure and did not reach an apparent steady-state. The half-life for acetone excretion by the lung was calculated to be 4.3 h and pulmonary excretion accounted for about 15 to 26% of the amount absorbed. Only about 1% of the absorbed acetone was excreted unchanged in the urine. The average half-life for acetone elimination from venous and arterial blood was 3.9 and 6.1 h, respectively. The amount of acetone taken up in the body was greater in the exercising subjects because of their higher ventilation rates.

Reference — Wigaeus, E., Löf, A., and Nordqvist, M.B. (1984). Uptake, distribution, metabolism, and elimination of styrene in man. A comparison between single exposure and co-exposure with acetone. Br. J. Ind. Med. 41:539-546.

Remark — The pharmacokinetics of acetone was examined using

resting and exercising volunteers exposed by inhalation to intentionally varying vapor concentrations of acetone that ranged from 21 to 211 ppm (56 to 500 mg/m^3) for periods of 4 h or less. The average relative uptake of acetone was found to be 54% for the subjects at rest and 53% for the individuals performing light physical exercise. In all treatment groups, a strong linear cor-relation was observed between the inhaled concentration of acetone and the end-exposure concentrations in the blood (r=0.86 to 0.99) and alveolar air (r=0.91). A good linear relationship was also observed between the inhaled acetone concentration and the concentration in the urine. The amount of acetone taken up by the lungs was shown to be strongly dependent upon the rate of pulmonary ventilation.

Reference

Pezzagno, G., Imbriani, M., Ghittori, S., Capodaglio, E., and Huang, J. (1986). Urinary elimination of acetone in experimental and occupational exposure. Scand. J. Work Environ. Health 12:603-608.

Pezzagno, G., Imbriani, M., Ghittori, S., and Capodaglio, E. (1988).Urinary concentration, environmental concentration, and respiratory uptake of some solvents: Effect of the work load. Am. Ind. Hyg. Assoc. J. 49:546-552.

Remark

Post-exposure concentrations of acetone in expired air and urine specimens were determined in subjects exposed to 200 to 600 ppm of acetone for 2-4 h on three consecutive days. The urine and expired air concen-trations were generally found to be proportional to the exposure concentration. Urine acetone levels were at a maximum 2-4 h after exposure termination and returned to normal within 16-18 h.

Reference

Tada, O., Nakaaki, K., and Fukabori, S. (1972). An experimental study on acetone and methyl ethyl ketone concentrations in urine and expired air after exposure to those vapors. J. Sci. Labour 48:305-336.

Remark

The blood levels of acetone in male volunteers exposed to acetone vapor concentrations of 100 or 500 ppm for 2 h were found to increase throughout the exposure. Steady-state blood levels were not attained at either exposure concentration. Peak end-exposure blood levels of

acetone were 2 and 10 mg/L for the 100 and 500 ppm exposures, respectively. The rate of acetone elimination from the blood was judged to be independent of the blood concentration (i.e., apparently zero-order). A first-order half-life of about 3 h was calculated.

Reference DiVincenzo, G.D., Yanno, F.J., and Astill, B.D. (1973). Exposure of man and dog to low concentrations of acetone vapor. Am. Ind. Hyg. Assoc. J. 34:329-336.

Remark A physiologically based pharmacokinetic model has been developed that describes the absorption, distribution, and elimination of acetone following inhalation exposure. The model includes eight tissue groups and incorporates actual physiologic, metabolic, and pharmacokinetic data to build differential equations that describe the kinetic behavior of acetone. The model was validated against actual human data and used to predict changes in acetone tissue concentration following 7-h occupational ex-posures to concentrations ranging from 10 to 2000 ppm.

Reference Kumagai, S. and Matsunaga, I. (1995). Physiologically based pharmacokinetic model for acetone. Occup. Environ. Med. 52:344-352.

Remark The rates of acetone production were measured in obese and nonobese humans during starvation-induced ketonemia. Three groups of human volunteers were given a small iv dose of 2[C^{14}]-acetone (1.01 to 2.72 µmmol) following a prolonged fast. Radioactivity from the administered acetone was detected in plasma glucose, lipids, and proteins, but not in plasma free fatty acids, acetoacetate, or β-hydroxybutyrate. A linear first-order decline in plasma radioactivity was observed while acetone blood levels remained constant.

Reference Reichard, G.A., Haff, A.C., Skutches, C.L., Holroyde, C.P., and Owen, O.E. (1979). Plasma acetone metabolism in the fasting human. J. Clin. Invest. 63:619-626.

Remark The pharmacokinetics of endogenous acetone was determined in patients with moderate to severe diabetic ketoacidosis. Adult patients were administered a small tracer dose (0.75 to 1.56 mmol) of 2[C^{14}]-acetone by iv bolus injection. The initial mean plasma acetone concentration in the patients was 4.96 mM (288 mg/L) with

a range of 1.55 to 8.91 mM (90 to 517 mg/L). The rate of acetone turnover in the body was found to range from 68 to 581 µmmol/min-1.73m^2 (values normalized to the body surface area of a standard human) and the rate was shown to be unrelated to the acetone plasma concentration. When the plasma acetone concentration was below 5 mM (290 mg/L), there was a direct linear relationship between the rate of endogenous acetone formation and the amount present in the plasma; however, at higher plasma levels there was marked decrease in acetone production. The excretion of acetone in the expired air accounted for about 20% of the production rate at plasma levels below 5 mM, but then increased to about 80% when the plasma concentration was higher.

Reference — Owen, O.E., Trapp, V.E., Skutches, C.L., Mozzoli, M.A., Hoeldtke, R.D., Boden, G., and Reichard, Jr., G.A. (1982). Acetone metabolism during diabetic ketoacidosis. Diabetes 31:242-248.

Remark — The preceding study was repeated using ketoacidotic diabetics administered 5.7 to 6.7 µmmol of 2[C^{14}]- acetone by constant iv infusion rate rather than bolus injection. The radiolabeled acetone was infused over a 4-h period in order to maintain steady-state levels of radioactivity in the plasma. The initial average concentration of acetone in the plasma was measured at 3.26 mM (189 mg/L) and ranged from 0.50 to 6.02 mM (29 to 349 mg/L) for the individual subjects. A minimum of 0.5-4.1% of the plasma glucose from the treated patients was found to be derived from endogenously produced acetone. The acetone turnover rate was found to be linearly related to the plasma concentration up to a level of 7.61 mM (442 mg/L).

Reference — Reichard, G.A., Skutches, C.L., Holroyde, C.P., and Owen, O.E. (1986). Acetone metabolism in humans during diabetic ketoacidosis. Diabetes 35:668-674.

Remark — Acetone was not absorbed through the skin of eight volunteers exposed to a saturated atmosphere of acetone vapor. Except for the head, the entire skin surface of each subject was exposed to both liquid acetone and acetone vapors by sitting in a sealed chamber for 20 to 30 min. Skin absorption was measured by comparing acetone blood levels before and after treatment.

Reference Cesàro, A.N. and Pinerolo, A. (1947). Sull'assorbimento percutaneo dell'acetone. Med. Lav. 38:384-387.

Remark Rapid skin penetration was reported when acetone was applied to a 12.5 cm^2 area of skin of volunteers exposed on four consecutive days. Acetone concentration ranges in the blood, urine, and expired air were 5 to 12 mg/L, 8 to 14 mg/L, and 5 to 12 ppm, respectively. The values increased by 3 to 5 fold when the exposure duration was increased from 2-4 h/day. The pulmonary excretion of absorbed acetone predominated over urinary excretion.

Reference Fukabori, S., Nakaaki, K., and Tada, O. (1979). On the cutaneous absorption of acetone. J. Sci. Labour 55:525-532.

Remark The uptake and excretion of acetone was determined in shoe factory workers where the instantaneous workroom concentration ranged from 0.5 to 21.1 ppm (1.1 to 49.9 mg/m^3). Calculation of the relative uptake at 1, 2.75, and 4.5 h gave values of 81, 81, and 71%, respectively. Acetone blood levels ranged between 0.47 and 3.0 mg/L, which were within physiologically normal limits. The acetone concentration in alveolar air was well correlated with the ambient air levels of acetone.

Reference Brugnone, F., Perbellini, L., Grigolini, L., and Apostoli, P. (1978). Solvent exposure in a shoe upper factory. I. n-Hexane and acetone concentration in alveolar and environmental air and in blood. Int. Arch. Occup. Environ. Health 42:51-62.

Brugnone, F., Perbellini, L., Gaffuri, E., and Apostoli, P. (1980). Biomonitoring of industrial solvent exposures in workers' alveolar air. Int. Arch. Occup. Environ. Health 47:245-261.

Remark The concentration of acetone in urine, blood, and alveolar air were determined for a group of 110 occu-pationally-exposed subjects. The 8-h TWA exposure concentrations of acetone in the workroom air ranged from about 10 to 1200 ppm, with an average of 372 ppm. Significant correlations were found between the exposure concentration and the level of acetone in urine, blood, and expired air. The best correlation coefficient (r=0.71) was obtained when the

workroom exposure concentration was evaluated against the acetone concen-tration in the urine. A TWA acetone exposure of 750 ppm was found to correspond to an end-of-shift urine acetone value of 76.6 mg/L.

Reference: Fujino, A., Satoh, T., Takebayashi, T., Nakashima, H., Sakurai, H., Higashi, T., Matumura, H., Minaguchi, H., and Kawai, T. (1992). Biological monitoring of workers exposed to acetone in acetate fibre plants. Br. J. Ind. Med. 49:654-657.

Remark: The urinary excretion of acetone was determined in 104 workers from three different factories (paint, plastics, and artificial fibers) where the 4-h TWA acetone expo-sures ranged as high as 1500 ppm. A good linear rela-tionship was when the 4-h urine acetone levels and the 4-h TWA exposure concentrations were compared (r=0.91). Urinary acetone levels were shown to be a good biomonitor of acetone exposures in the workplace. A urine acetone concentration of 54 mg/L was shown to equal a 4-h TLV-TWA exposure to 1000 ppm of acetone.

Reference: Pezzagno, G., Imbriani, M., Ghittori, S., Capodaglio, E., and Huang, J. (1986). Urinary elimination of acetone in experimental and occupational exposure. Scand. J. Work Environ. Health 12:603-608.

Pezzagno, G., Imbriani, M., Ghittori, S., and Capodaglio, E. (1988). Urinary concentration, environmental concentration, and respiratory uptake of some solvents: Effect of the work load. Am. Ind. Hyg. Assoc. J. 49:546-552.

Remark: The relationship between urinary acetone levels and the 8-h TWA exposure concentration was examined in a group of 28 workers in a plastics plant. A good corre-lation was found between the TWA exposure level and the end-exposure concentration of acetone in the urine (r=0.90). Urine acetone levels ranged from about 0.5 to 23 mg/L for employees whose personal 8-h TWA exposure concentration ranged from less than 1 ppm to about 45 ppm.

Reference: Kawai, T., Yasugi, T., Uchida, Y., Iwami, O., and Ikeda, M. (1990). Urinary excretion of unmetabolized acetone as an indicator of occupational exposure to acetone. Int. Arch.

Occup. Environ. Health 62:165-169.

Kawai, T., Yasugi, T., Mizunuma, K., Horiguchi, S., Iguchi, H., and Ikeda, M. (1992). Curvi-linear relation between acetone in breathing zone air and acetone in urine among workers exposed to acetone vapor. Toxicol. Lett. 62:85-91.

Remark	Acetone was detected in the expired air and saliva of a female exposed to 600 and 2500 ppm of acetone for 15 min. Peak saliva acetone concentrations of approximately 4 and 16 g/mL were measured after the 600 and 2500 ppm exposures respectively. Saliva and exhaled air concentrations of acetone were well correlated (r=0.82) with the concentrations in saliva exceeding those in expired air.
Reference	Tomita, M. and Nishimura, M. (1982). Using saliva to estimate human exposure to organic solvents. Bull. Tokyo Dent. Coll. 23:175-188.