Appendix A

OECD SIDS Dossier and SIAR for Acetone

SIDS Initial Assessment Report (SIAR) for the 9th SIAM

Place: Paris, France Date: June 29-30, 1999
July 1, 1999

Chemical Name: Acetone

CAS No: 67-64-1

Sponsor Country: USA

National SIDS Contact Point in Sponsor Country:

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HISTORY:

This high production volume (HPV) chemical was assigned to the USA in Phase 4 of the OECD HPV voluntary testing program. A SIDS Dossier was prepared by the Chemical Manufacturer's Association and submitted to the National SIDS Contact Point (USA) on March 14, 1997. The draft SIAR was reviewed on March 7, 1998 at SIAM 7 and again on October 28, 1998 at SIAM 8. Modifications were made in accordance with the comments received from the participants.

COMMENTS:

Deadline for Circulation:

Date of Circulation:

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	67-64-1
CHEMICAL NAME	Acetone
STRUCTURAL FORMULA	CH_3-CO-CH_3

RECOMMENDATIONS OF THE SPONSOR COUNTRY

Environment

The chemical is generally of low toxicity to aquatic organisms and is considered to be readily biodegradable. It is currently considered to be slightly hazardous and of low priority for further work.

Health

This chemical is an eye irritant and has an acute effect on the central nervous system through inhalation route. However, high exposures are required and health hazards are slight, so the priority for further work is low.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE RECOMMENDATIONS

Worldwide production capacity of acetone was 3.8 million tonnes in 1995 with the actual volume produced being somewhat less at 3.7 million tonnes. Production capacity in the United States constituted about 33% (1.3 million tonnes) of the global capacity, while Western Europe and Asia (including Japan) were about 31% (1.2 million tonnes) and 19% (0.7 million tonnes), respectively. Major end uses of acetone can be divided into three separate categories as: i) a chemical feedstock, ii) a formulating solvent for commercial products, and iii) an industrial process solvent.

PECs have been derived based on the results from air and water monitoring data. The PEC_{local} (2500 μg/L [water], 10,000 μg/m^3 [air]) and PEC_{global} (50 μg/L [water], 10 μg/m^3 [air]) values are intended to represent plausible worst case environment concentrations on a global and regional scale.
High concentrations of acetone can be detected in a variety of occupational environments (up to 2876 mg/m^3 at cellulose acetate factory). The predominant route of both occupational and consumer exposure is through vapor inhalation. The estimated human exposure (EHE) value for workplace employees is 1780 mg/m^3. Acetone can be found in wide variety of consumer and commercial products but only a few are known to contain high concentrations. These include paints and paint-related products, such as paint thinners, finger nail polish removers, automotive waxes and tar removers. Using a USEPA modelling programme entitled SCIES (Screening Consumers Inhalation Exposure Software), a scenario intended to represent a likely indoor consumer use of a product (45 min application of a spray contact adhesive that contained 21% acetone) predicted a short-term exposure (EHE) value of 900 mg/m^3 for the consumer use of the product.

An assessment factor of 100 was used to calculate a predicted no effect concentration (PNEC) for acetone in an aqueous environment, since acute toxicity data were available for algae, crustaceans,

and fish. The lowest PNEC value for these species was calculated to be 21 mg/L when using the LC_{50} value of 2100 mg/L for marine brine shrimp. The PEC_{local} and PEC_{global} values for water were 2500 μg/L and 50 μg/L, respectively.

The scientific literature contains eight different studies that have measured either the neuro-behavioural performance or neurophysiological response of humans exposed to acetone. Effect levels ranging from about 600 to greater than 2375 mg/m^3 have been reported. Neurobehavioral studies with acetone-exposed employees have recently shown that 8-hr exposures in excess of 2375 mg/m^3 were not associated with any dose-related changes in response time, vigilance, or digit span scores. The subchronic toxicity of acetone has been examined in mice and rats that were administered acetone in the drinking water and again in rats treated by oral gavage. Acetone-induced increases in relative kidney weight changes were observed in male and female rats used in the oral 13-week study. Acetone treatment caused increases in the relative liver weight in male and female rats that were not associated with histopathologic effects and the effects may have been associated with microsomal enzyme induction. Hematologic effects consistent with macrocytic anemia were also noted in male rats along with hyperpigmentation in the spleen. The most notable findings in the mice were increased liver and decreased spleen weights. Overall, the no-observed-effect-levels in the drinking water study were 1% for male rats (900 mg/kg/d) and male mice (2258 mg/kg/d), 2% for female mice (5945 mg/kg/d), and 5% for female rats (3100 mg/kg/d). For developmental effects, a statistically significant reduction in foetal weight, and a slight, but statistically significant increase in the percent incidence of later resorptions were seen. The no-observable-effect level for developmental toxicity was determined to be 5220 mg/m^3 for both rats and mice. Lifetime dermal carcinogenicity studies in mice treated with up to 0.2 mL of acetone did not reveal any increase in organ tumor incidence relative to untreated control animals.

Clinical case studies, controlled human volunteer studies, animal research, and occupational field evaluations all indicate that the NOAEL for this effect is 2375 mg/m^3 or greater. The EHE/NOAEL ratio for the neurological effects indicates a margin of exposure of 0.75 for occupational use and 0.40 for the consumer use of acetone. The NOAEL of 900 mg/kg/d from the subchronic drinking study was used together with an assuming pulmonary uptake of 50% and a human ventilation rate of 21.6 m^3/d for consumer exposures and 10 $m^3/8hr$ for occupational exposures to calculate an inhalation NOAEL. The drinking water NOAEL was found to be equivalent to a 24-hr consumer inhalation exposure of 5833 mg/m^3 and an 8-hr occupational exposure of 12,600 mg/m^3. For developmental effects, the NOAEL was 5220 mg/m^3.

IF FURTHER WORK IS RECOMMENDED - INDICATE ITS NATURE

FULL SIDS SUMMARY

CAS NO: 67-64-1		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Freezing. Point			-94.6 °C
2.2	Boiling Point			56.1 °C at 760 mm Hg
2.3	Vapor Pressure			182 mm Hg at 20 °C 400 mm Hg at 39.5 °C
2.4	Partition Coefficient			-0.24 (Log Kow)
2.5	Water Solubility			100% at 20 °C
2.6	Flash Point			Cleveland open cup : -9 °C Tag closed cup : -17 °C
2.7	Flammability			Lower limit : 2.2% (v/v) at 25 °C Upper limit : 13.0% (v/v) at 25 °C
2.8	Autoignition Temperature			465 °C
2.9	Specific Gravity			0.791 at 20 °C
ENVIRONMENTAL FATE/BIODEGRADATION				
3.1.1	Photodegradation		Calculated Calculated	Undergoes slow photolysis Water: $T_{1/2}$ >43 hr Air : $T_{1/2}$ = 80 hr
3.1.2	Stability in Water		SRC Program	Does not hydrolyze
3.1.3	Stability in Soil		SRC Program	Log K_{OC} = 0.30 (Calculated)
3.2	Monitoring Data			Water (μg/L): residential well water : 2 - 7 sea water : 5 - 53 ground water : 12 - 25 lake water : 1 - 50 storm water runoff : 0 - 100 cloud water : 0 - 17,300 industrial wastewater : 138 - 37,709 landfill leachate : 50 - 62,000 Air ($\mu g/m^3$): inside office building : 7.1 - 28.5 inside home : 9.5 - 81 urban street : 2.4 - 306 nonsmoking workplace : 4.7 - 415 inside aircraft cabin : 7.1 - 560 human breath : 230 - 11,285 smoking workplace : 9.5 - 21,085

FULL SIDS SUMMARY (con't)

CAS NO: 67-64-1		SPECIES	PROTOCOL	RESULTS
ENVIRONMENTAL FATE/BIODEGRADATION				
3.3	Transport/Distribution		Fugacity Level 1	Distribution: Air : 71.0% Water : 28.6% Soil : 0.0%
			Calculated Measured	Partition Coefficients: Octanol/Water : 0.58 Water/Air : 334
3.4	Type of Biodegradation			aerobic anaerobic
3.5	Biodegradation		OECD 301D	Freshwater: BOD_5 : 14% BOD_{15} : 74% BOD_{28} : 74% Seawater : BOD_5 : 38% BOD_{10} : 67% BOD_{15} : 69% BOD_{20} : 76%
3.6	Oxygen Demand			Theoretical (ThOD): 2.20 g O_2/g Chemical (COD) : 2.00 g O_2/g
3.7	Bioconcentration			Atlantic Cod BCF : 0.65
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish			LC_{50} (mg/L) : Fathead minnow : 15,000 Japanese medaka : 14,300 Mosquito fish : 13,000 Goldfish : >5000 Golden orfe : 9880 Bluegill sunfish : 8300 Rainbow trout : 7400 Brook trout : 6070
4.2	Acute Toxicity to Aquatic Invertebrates			LC_{50} (mg/L) : *Nitocra spinipes* : 16,700 *Daphnia magna* : 15,800 *Daphnia pulex* : 8800 *Daphnia cucullata*: 7635 *Artemia salina* : 2100
4.3	Toxicity to Aquatic Plants			NOEC (mg/L) : *Scenedesmus quadricauda* : 7500 *Selenastrum capricornutum* : 7000 *Chlorella pyrenoidosa* : 3400 *Scenedesmus pannonicus* : 4740 *Lemna gibba* : 5400 *Lemna minor* : 5400

FULL SIDS SUMMARY (con't)

CAS NO: 67-64-1		SPECIES	PROTOCOL	RESULTS
ECOTOXICOLOGY				
4.4	Toxicity to Bacteria, Diatoms, and Protozoa			NOEC (mg/L) : *Escherichia coli* : 25,000 *Nitzschia linearis* : 11,610 *Skeletonema costatum* : 6000 *Chilomonas paramecium* : 3520 *Uronema parduczi* : 1710 *Pseudomonas putida* : 1700 *Microcystis aeruginosa* : 530 *Entosiphon sulcatum* : 28
4.5.2	Chronic Toxicity to Aquatic Invertebrates			NOEC (mg/L) : *Ceriodaphnia dubia* : 1866 *Daphnia magna* : 1660
4.6.1	Toxicity to Soil Dwelling Organisms		Predicted	NOEC (mg/L) : *Lumbricus terrestris* : >1000
4.6.2	Toxicity to Terrestrial Plants			NOEC (mg/L) : Ryegrass : >80 Radish : >80 Lettuce : >80 Corn : >80
4.6.3	Toxicity to Other Non-Mammalian Terrestrial Species			NOEC (mg/kg) : Japanese quail : >40,000 ring-neck pheasant : >40,000
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	rat mouse rabbit		LD_{50} : 8400 mg/kg LD_{50} : 5250 mg/kg LD_{50} : 5300 mg/kg
5.1.2	Acute Inhal. Toxicity	rat		LC_{50} : 50,000 mg/m^3
5.1.3	Acute Dermal Toxicity	rabbit		LD_{50} : >15,700 mg/kg
5.2.1	Skin Irritation	rabbit		not irritating
5.2.2	Eye Irritation	rabbit	Draize	highly irritating
5.2.3	Respiratory Irritation	mouse	RD_{50}	weakly irritating
5.3	Sensitization	mouse	ear swelling	not sensitizing

FULL SIDS SUMMARY (con't)

CAS NO: 67-64-1		SPECIES	PROTOCOL	RESULTS
TOXICOLOGY				
5.4	Repeated Dose Toxicity	mice : male mice : female	OECD 408	NOEL : 1% (2258 mg/kg/day) 2% (5945 mg/kg/day)
		rat : male rat : female	OECD 408	NOEL : 1% (900 mg/kg/day) 5% (3100 mg/kg/day)
5.5	Genetic Toxicity In Vitro		OECD 471	bacterial test: reverse mutation : neg. At 10 mg yeast gene mutation : neg. at 5% forward mutation : neg. At 500 mM prophage induction : neg. at 10% non-bacterial test : chromosomal aberration : neg. at 5 mg/mL sister chromatid exchange : neg. at 5 mg/mL cell transformation : neg. at 0.5% alkaline elution : neg. at 1% mouse lymphoma : neg. At 30 mg/mL chromosomal malsegregation : pos. at 6.8%
5.6	Genetic Toxicity In Vivo	rat mouse hamster	OECD 474	embryo cell transformation assay : rat : negative at 0.1% mouse : negative at 0.01% micronucleus assay : negative at 865 mg/kg
5.7	Carcinogenicity	mouse		NOEL : 0.2 mL (dermal)
5.8	Toxicity to Reproduction	rat		NOEL : 0.5% (drinking water)
5.9	Developmental Toxicity/ Teratogenicity	mouse	OECD 414	NOEL : teratogenicity : >26,110 mg/m^3 developmental : 5220 mg/m^3
			OECD 414	NOEL : teratogenicity : >15,665 mg/m^3 developmental : 5220 mg/m^3
5.11	Experience with Human Exposure			see SIAR text

1. IDENTITY

Acetone is a clear colorless liquid that is highly flammable and infinitely soluble with water. Reagent grade acetone can contain up to 0.5% water as well as small amounts of other polar solvents. Acetone vapors have a characteristic sweet and fruity odor at low concentrations. The odor threshold for humans has been reported at values ranging from about 24 to 1615 mg/m^3, with 235 to 339 mg/m^3 being the range of odor recognition thresholds for most people and 95 mg/m^3 being the odor detection threshold for unadapted individuals (Devos *et al*., 1990; Leonardos *et al*., 1969).

Virtually every organ and tissue within the human body contains some acetone which is one of three biochemicals collectively referred to as ketone bodies. Acetone is produced within the body as a result of the breakdown and utilization of stored fats and lipids as a source of energy (Wieland, 1968). Consequently, conditions such as strenuous physical exercise and prolonged dieting, which lead to a break-down of fat within the body, may result in higher than average amounts of acetone in the bloodstream (Williamson and Whitelaw, 1978). Measurable amounts of acetone are continuously being excreted in the breath and urine of humans as a result of its high volatility and solubility in water (Wigaeus *et al*., 1981).

2. GENERAL INFORMATION ON EXPOSURE

Worldwide production capacity of acetone was 3.8 million tonnes in 1995 with the actual volume produced being somewhat less at 3.7 million tonnes (Bizzari, 1996). Production capacity in the United States constituted about 33% (1.3 million tonnes) of the global capacity, while the capacity in Western Europe and Asia (including Japan) was about 31% (1.2 million tonnes) and 19% (0.7 million tonnes), respectively. The average annual production of acetone is expected to rise at a global rate of 3.3% until the year 2000.

Major end uses of acetone can be divided into three separate categories. These include use as: i) a chemical feedstock, ii) a formulating solvent for commercial products, and iii) an industrial process solvent. The majority of worldwide production is used as a feed-stock to prepare methyl methacrylate/methacrylic acid and Bisphenol A (Bizzari, 1996). Several aldol chemicals, such as methyl isobutyl ketone, methyl isobutyl carbinol, isophorone, and diacetone alcohol, are also prepared directly from nascent acetone. Acetone has many favorable properties that make it useful as a formulating solvent for a variety of paints, inks, resins, varnishes, lacquers, surface coatings, paint removers, and automotive care products. As an industrial process solvent, acetone is used to manufacture cellulose acetate yarn, polyurethane foam, vitamin C, and smokeless gun powder. At least 75% of the acetone consumed in 1995 was used in captive processes for the preparation of downstream chemicals, while only about 12% was used as a formulating solvent for commercial products.

Large-scale commercial production of acetone is generally accomplished by one of two processes. The first, and by far the most common, is through the acid catalyzed hydro-lytic cleavage of cumene hydroperoxide (Bizzari, 1996). Acetone and phenol are formed as co-products in this reaction at a ratio of 0.61 to 1.00. The second process, catalytic

dehydrogenation of isopropyl alcohol, accounted for about 6% of the US production in 1995. Other methods, such as biofermentation, propylene oxidation, and diisopropyl-benzene oxidation, are either experimental in nature or account for a very small percentage of worldwide production.

The release of acetone by chemical manufacturers' and end users accounts for a very small percentage (1%) of the estimated 40 million tonnes that are annually released to the environment (Table 1). Vegetative releases, forest fires, and other natural events account for nearly half (47%) of the estimated annual emissions of acetone, with another 50% resulting from the tropospheric photooxidation of propane and other alkanes and alkenes (Singh *et al*., 1995). Since 1993, US industries have not been required to report their TRI (Toxic Release Inventory) emissions of acetone as required under SARA Title III, Section 313. In 1992, 2548 facilities reported a total environmental release of 60,904 tonnes of acetone with 60,904 tonnes emitted to the air, 454 tonnes to water, 254 tonnes to land, and 1446 tonnes injected underground (USEPA, 1994).

Table 1
Estimated average annual emissions of acetone from different sources

Acetone Source	Global Annual Emissions (tonnes x 10^{-6}) Average	Range
Primary Anthropogenic		
stationary sources	0.5	0.4 - 0.7
mobile sources	0.3	0.2 - 0.3
Primary Biogenic		
vegetation	9	4 - 18
Secondary Anthropogenic &		
propane oxidation	17	15 - 20
isobutane & isopropane oxidation	2	1 - 3
isobutene & isopropene oxidation	1	1 - 2
myrcene oxidation	0.2	0.2 - 0.3
Biomass Burning	10	8 - 12
Total	40	30 - 46

Acetone can be found as an ingredient in a variety of consumer products ranging from cosmetics to processed and unprocessed foods. Acetone has been rated as a GRAS (Generally Recognized as Safe) substance when present in beverages, baked goods, deserts, and preserves at concentrations ranging from 5 to 8 mg/L (Oser and Ford, 1973). It can also be detected in measurable amounts in onions, grapes, cauliflower, tomatoes, milk, cheese, beans, peas, and other natural foods. Milk from dairy cattle may contain very high levels of acetone, ranging as high as 225 mg/L for the milk from hyperketo-nemic cows (Andersson and Lundström, 1984). Acetone has also been identified, but not quantified, in air samples from numerous plants and microorganisms. In addition to its elimination in the expired air of all mammals, acetone is excreted as a metabolic end-

product by some bacteria (*Clostridium butylicium*), molds, fungi (*Paecilaomyces variotii*), and algae (*Cryptomonas ovata palustris*) (George *et al*., 1983; Sunnesson *et al*., 1996; Collins and Kalnins, 1966).

Acetone is often detected as an end product of thermal combustion and biological decomposition. Except for tree foliage, the release of acetone from living vegetation has been poorly quantified (Khalil and Rasmussen, 1992). Emissions from poultry manure (530 g/kg), backyard waste incinerators (4.0 g/kg), pine wood combustion (2.8 g/kg), neoprene combustion (990 mg/kg), and wood burning stoves (145 mg/kg) have all been measured and reported (Smith *et al*., 1977; Yocum *et al*., 1956; Hartstein and Forshey, 1974; Lipari *et al*., 1984).

3. ENVIRONMENT

3.1 Environmental Exposure

3.1.1 *General Discussion*

A level I fugacity analysis revealed that acetone preferentially locates in the air compartment when released to the environment (Table 2). The fugacity analysis was based on the equilibrium established after the release of 100 moles (5.8 kg) of acetone into the envi-ronment (Mackay and Paterson, 1981). A substantial amount of acetone can also be found in water, which is consistent with the high water to air partition coefficient and its small, but detectable, presence in rain water, sea water, and lake water samples. Very little acetone is expected to reside in soil, biota, or suspended solids. This is entirely consistent with the physical and chemical properties of acetone and with measurements showing a low propensity for soil absorption and a high preference for moving through the soil and into the ground water (Steinberg and Kreamer, 1993).

Table 2
State-state distribution of acetone in the environment

Environmental Compartment	Mass Distribution (%)
air	71.00
water	28.58
sediment	0.01
soil	0.00
biota	0.00
suspended solids	0.00

Acetone meets the OECD definition of readily biodegradable which requires that the biological oxygen demand (BOD) is at least 70% of the theoretical oxygen demand (THOD) within the 28-day test period (Table 3). Studies by the standard dilution method have shown greater than 75% of the acetone is biodegraded when using non-acclimated

sewage seed from either a freshwater or a sea water sanitary waste treatment plant. These results compare favorably with the values from biodegradability tests performed according to OECD 301D guidelines. Using the OECD method, the BOD_5, BOD_{15}, and BOD_{28} for acetone were found to be 14%, 74%, and 74%, respectively (Waggy *et al*., 1994). The BOD_5 of acetone has been measured by numerous investigators and produced values ranging from about 23% to 83% depending on the test and the type of sewage seed. The THOD of 2.20 g O_2/g of acetone has been found to be only slightly greater than the measured chemical oxygen demand (COD) value of 2.00 g O_2/g of acetone (Price *et al*., 1974).

Table 3
The biological oxygen demand from acetone in water samples

Sample Type	Biological Oxygen Demand (g)				Author(s) (year)
	5 days	10 days	15 days	20 days	
freshwater	55	79	78	78	Lamb & Jenkins, 1952
freshwater	56	76	83	84	Price *et al*., 1974
saltwater	38	67	69	76	Price *et al*., 1974

Studies with several different strains of anaerobic bacteria from municipal waste water treatment plants have shown that acetone is completely degraded to CO_2 following aceto-acetate formation through an initial carboxylation reaction and incorporated into the carbon cycle (Platen and Schink, 1989). Soil bacteria have also been shown to biodegrade acetone to CO_2 (Taylor *et al*., 1980).

Table 4
Comparison of the environmental fate and removal processes for acetone

Acetone Removal Process	Approximate Half-life (days)	Author(s) (year)
aqueous biodegradation	0.6	Rathbun *et al*., 1993
volatilization river	6	Howard *et al*., 1990
soil biodegradation	7	Sanders, 1995
total tropospheric removal	22	Meyrahn *et al.*, 1986
hydroxyl radical reaction	31	Meyrahn *et al.*, 1986
aqueous photolysis	40	Betterton, 1991
atmospheric photolysis	80	Meyrahn *et al.*, 1986
volatilization lake	100	Howard *et al*., 1990

Two processes govern the photochemical removal of acetone from the troposphere: reaction with hydroxyl radicals and photolysis. The two processes occur at about equal rates in clear unpolluted skies yielding a total tropospheric lifetime of about 32 days (Meyrahn *et al*., 1986). The reaction with hydroxyl radicals will predominate over photolysis in urban areas where hydroxyl radical concentrations are greater, and during cloudy

winter-time conditions where photodecomposition is minimal. Rain out and other forms of wet deposition are considered to be minor tropospheric removal processes (Chatfield *et al*., 1987). Calculated and measured rate constants have been used to estimate the elimination half-life ($t_{½}$= 0.693/k_{calc}) of acetone through various environmental processes (Table 4). These data show that acetone is rapidly biodegraded in water and that this is the dominant removal process in the environment. The slow removal of acetone from the troposphere indicates that it is relatively non-reactive and a minor contributor to urban ozone and peroxyacyl nitrate (PAN) concentrations (Derwent *et al*., 1996).

3.1.2 *Predicted Environmental Concentration*

Measurable amounts of acetone can be found in both mobile and stationary emission sources (Table 5). The levels of acetone in the air from municipal landfills and cigarette smoke can be relatively high, but they are minor contributors to the total global mass. The direct release of acetone from vegetation is an important emission source that is often overlooked. In a qualitative evaluation, acetone was found to be emitted from all 22 of the forest plant species examined (Isidorov *et al*., 1985).

Table 5
Mobile and stationary emissions of acetone

Emission Source	Airborne Concentration (mg/m^3)	Author(s) (year)
fuel or crude oil fire	0.02 - 0.16	Booher & Janke, 1997
automobile exhaust	0.09 - 4.50	Grimaldi *et al*., 1996
factory fence line	1.9 - 9.7	Hoshika *et al.*, 1981
tree foliage	7.8 - 12.6	Khalil & Rasmussen, 1992
municipal landfill	15.7 - 77.1	Brosseau & Heitz, 1994
cigarette smoke	498 - 869	Euler *et al*., 1996

Background levels of acetone in the atmosphere have been assessed from both ground level and airborne monitoring stations located throughout the world. The average acetone concentrations at rural ground level sites are generally lower than the values reported for urban areas (Table 6). The concentration of acetone in urban areas can show large unpre-dictable variations that are likely related to the amount of vehicle traffic and to the emis-sion of precursor alkanes and alkenes (Zweidinger *et al*., 1988; Chatfield *et al*., 1987). Airborne measurements of acetone in the upper troposphere and lower stratosphere reveal an average concentration of 190 to 285 ng/m^3 in these regions (Singh *et al*., 1995).

Acetone has routinely been detected in the expired air of humans and in the air samples from many different occupied environments (Table 7). The levels in these samples can vary greatly, ranging from a few $\mu g/m^3$ to nearly 25 mg/m^3. Cigarette smoking, emissions from furnishings and construction materials, and excretion by the lung are

perhaps the greatest contributors to indoor acetone levels. The acetone levels in indoor air are generally higher than those found outdoors (Jarke *et al*., 1981).

Table 6
Background levels of acetone in urban and rural air samples

Location	Background Concentration (μg/m^3)	Range (μg/m^3)	Author(s) (year)
Smoky Mts, Tennessee	---	1.7 - 9.5	Arnts & Meeks, 1981
Copenhagen, Denmark	---	0.5 - 5.2	Granby *et al.*, 1997
Point Barrow, Alaska	2.4	0.7 - 6.9	Cavanagh *et al.*, 1969
Waldhof, Germany	3.8	---	Solberg *et al*., 1996
Central Ontario	4.0	---	Shepson *et al.*, 1991
Eastern Georgia	4.3	0.0 - 15.9	Lee *et al.*, 1995
Los Angeles, California	3.8	0.2 - 15.2	Grosjean *et al*., 1996
Ispra, Italy	4.7	---	Solberg *et al*., 1996
Donan, France	4.7	---	Solberg *et al.*, 1996
Athens, Greece	---	1.7 - 18.3	Kalabokas *et al*., 1997
Columbus, Ohio	5.0	0.0 - 21.8	Spicer *et al*., 1996
Southern Germany	6.2	0.5 - 11.4	Slemr *et al*., 1996
Western Colorado	---	2.4 - 8.3	Goldan *et al*., 1995
Western Alabama	10.0	0.7 - 5.2	Goldan *et al.*, 1997
Sao Paulo, Brazil	---	0.5 - 7.4	Grosjean *et al.*, 1990
Rome, Italy	16.1	10.0 - 21.8	Possanzini *et al.*, 1996
Stockholm, Sweden	9.5	1.7 - 24.2	Jonsson *et al.*, 1985
Vancouver, Canada	19.2	8.3 - 30.9	Li *et al.*, 1997
Boston, Massachusetts	32.0	9.7 - 64.0	Kelly *et al.*, 1993
Houston, Texas	81.9	29.4 - 223.1	Kelly *et al.*, 1993

Table 7
Acetone concentration range in various airborne samples

Sample Type	Airborne Concentration (μg/m^3)	Author(s) (year)
inside office building	7.1 - 28.5	Daisey *et al*., 1994
inside home	9.5 - 81	Lewis & Zweidinger, 1992
urban street	2.4 - 306	Jonsson *et al.*, 1985
nonsmoking workplace	4.7 - 415	Heavner *et al*., 1996
inside aircraft cabin	7.1 - 560	Dechow *et al*., 1997
human breath	230 - 11,285	Crofford *et al.*, 1977
smoking workplace	9.5 - 21,085	Heavner *et al*., 1996

Fugitive stack emissions have been used to estimate fence line concentrations of acetone at three industrial sites. Airborne emissions reported under USEPA SARA Title III

section 313 for the year 1989 or 1990 were used in conjunction with the USEPAs ISCST (Industrial Source Complex Short Term) dispersion model to calculate the highest 24-hr concentration and the highest average annual concentration of acetone at property sites beyond the fence line (Table 8). The highest average annual concentration at the three industrial sites ranged from 4.3 to 9.3 mg/m^3. Actual fence line measurements of acetone at five locations outside of the Eastman Chemical Company site in Kingsport, Tennessee showed that the average concentration ranged from 0.05 to 0.50 mg/m^3 which were notably lower than the predicted 24-hr average.

Table 8
Fugitive emissions of acetone and the resulting maximum predicted off-property concentrations

Company & Location	Fence Line Concentration (mg/m^3)	
	24-hr average	annual average
Eastman Chemical Co. Kingsport, TN	0.9	9.3
Hoechst-Celanese Corp. Narrows, WV	2.6	8.3
Hoechst-Celanese Corp. Rock Hill, SC	0.1	4.3

Acetone has been found in surface and ground water samples at concentrations that were highly dependent on the type of sample (Table 9). Ambient background levels of acetone are the result of both natural and commercial releases and are generally reflective of the physical processes affecting absorption from the air, movement through soil, and microbial biodegradation. A search of the open literature and the nearly 2000 entries in USEPAs STORET database revealed that acetone levels in natural water and industrial monitoring wells rarely exceeded 1 mg/L.

Table 9
Acetone concentration range in different water samples

Sample Type	Aqueous Concentration (µg/L)	Author(s) (year)
residential well water	2 - 7	Dewalle & Chain, 1981
sea water	5 - 53	Corwin, 1969
ground water	12 - 25	Sabel & Clark, 1984
lake water	1 - 50	Jungclaus *et al*., 1978
storm water runoff	0 - 100	Line *et al*., 1997
cloud water	0 - 17,300	Aneja, 1993
industrial wastewater	138 - 37,709	Howard *et al*., 1990
landfill leachate	50 - 62,000	Brown & Donnelly, 1988

A USEPA-sponsored survey has determined the acetone concentrations in the discharge from 4000 industrial and publicly owned wastewater treatment plants (Table 10). The highest recorded individual concentration of 37.7 mg/L was found in the discharge from

a paint and ink industry facility; whereas, the highest median concentration of 2.5 mg/L was associated with printing and publishing plants (Howard *et al*., 1990). The highest reported aqueous acetone concentration was found in the wastewater from a specialty chemical manufacturing plant. Although wastewater acetone levels of about 200 mg/L were found in water samples from the primary influent at the wastewater treatment plant serving this manufacturing site, the levels in the receiving river water and sediment beyond the treatment plant were below the analytical detection limit (Jungclaus *et al*., 1978). These results are in agreement with data showing that 94% of the acetone removed by a pilot-scaled wastewater facility occurs during secondary treatment (Bhattacharya *et al*., 1996).

Table 10
Acetone concentrations in the discharge water from industrial and public wastewater treatment plants

Industrial Category	Number of Positive Occurrences	Median Acetone Concentration (µg/L)
nonferrous metal	2	6.6
textile mills	4	11.0
inorganic chemicals	8	13.8
porcelain/enameling	4	14.7
pesticide manufacturing	7	52.7
oil and gas extraction	5	59.2
pulp and paper	6	59.8
leather tanning	4	74.7
pharmaceuticals	6	75.4
mechanical products	6	84.4
photographic industries	1	94.9
publicly owned treatment works	40	96.8
organic chemicals	1	113.9
plastics and synthetics	10	164.1
petroleum refining	14	166.9
organics and plastics	24	374.4
explosives	23	388.0
auto and other laundries	2	437.5
electronics	12	441.2
rubber processing	1	604.4
transportation equipment	6	616.7
paint and ink	22	894.9
coal mining	1	2260.8
printing and publishing	7	2501.2

Predicted environmental concentrations (PECs) of acetone have been derived from the air and water monitoring data described above. The values listed in Table 11 have been taken from the published report that best provide a plausible worst case environmental

concentration on both a global and regional scale. The $PEC_{(local)}$ and $PEC_{(global)}$ air concen-trations of 10,000 and 10 μg/m^3 were based on factory fence line concentrations (Table 5; Hoshika *et al*., 1981) and ambient air concentrations for a remote region in the western US (Table 6; Golden *et al*., 1995), respectively. The $PEC_{(local)}$ and $PEC_{(global)}$ water con-centrations of 2500 and 50 μg/L represent the highest median acetone concentration from an industrial wastewater treatment plant (Table 10; Howard *et al*., 1990) and the highest reported natural water concentration of acetone from seawater (Table 9; Corwin, 1969).

Table 11
Predicted environmental acetone concentrations

Area	Concentration Air (μg/m^3)	Concentration Water (μg/L)
$PEC_{(local)}$	10,000	2500
$PEC_{(global)}$	10	50

3.2 Effects on the Environment

3.2.1 *Aquatic Effects*

As shown in Tables 12 and 13, acetone is minimally toxic to freshwater and marine organisms exposed for 1 to 10 days. Acute NOEC for vertebrate and invertebrate organisms were greater than 3500 mg/L and the LC_{50} values were generally greater than 10,000 mg/L. The marine brine shrimp (*Artemia salina*) showed the greatest sensitivity to acetone with a 1-day LC_{50} value of 2100 mg/L.

When examined at a seawater concentration of 1.52%, acetone did not bioconcentrate in the tissues or organs of the Atlantic cod (*Gadus morhua*) (Rustung *et al*., 1931). The 7-day EC_{50} values of greater than 10,000 mg/L and no observable effect levels of 5400 mg/L were similar for two species of aquatic duckweed, *Lemna gibba* and *Lemna minor* (Cowgill *et al*., 1991). The 10-day LC_{50} values for acetone in the 3-brood test with *Daphnia magna* and *Ceriodaphnia dubia* were 4068 mg/L and 6693 mg/L, respectively (Cowgill and Millazo, 1991). The maximum acceptable concentration of acetone that did not affect the survival of *Daphnia magna* exposed for 28 days was approximately 2100 μL/L (1660 mg/L) (LeBlanc and Surprenant, 1983).

3.2.2 *Terrestrial Effects*

The 5-day LC_{50} of acetone for Japanese quail (*Coturnix coturnix japonica*) and ring-neck pheasants (*Phasianus colchicus*) was greater than 40,000 mg/kg (Hill *et al*., 1975). The EPAs ECOSAR program predicted a 14-day earthworm (*Lumbricus terrestris*) LC_{50} value of greater than 1000 mg/L (Meylan and Howard, 1998). Acetone vapors were shown to be relatively toxic to two types insects and their eggs. The time to 50% lethality (LT_{50}) was found to be 51.2 hr and 67.9 hr when the flour beetle (*Tribolium confusum*) and the flour moth (*Ephestia kuehniella*) were exposed to an airborne acetone

concentration of 61.5 mg/m^3 (Tunç *et al*., 1997). The LT_{50} values for the eggs were 30-50% lower than for the adult. The direct application of acetone liquid to the body of the insects or surface of the eggs did not, however, cause any mortality.

The effects of acetone on the growth and germination of terrestrial plants and seeds has also been examined (Gorsuch *et al*., 1990). A 168-hr exposure of ryegrass (*Lolium perenne*), radish (*Raphanus sativus*), and lettuce (*Lactuca sativa*) to acetone concentrations as high as 80 mg/L did not cause any effects. The IC_{50} value obtained when tobacco pollen (*Nicotiana sylvestris*) was incubated with acetone for 18 hr was 20,500 mg/L (Kristen *et al*., 1994). This value, however, conflicts with the 2-hr NOEC of 12 mg/L for the germination of another tobacco plant species, *Nicotiana tabacum* (Schubert *et al*., 1995).

Table 12
Acute and chronic toxicity of acetone to aquatic invertebrates

Species	Duration (hr)	NOEC (mg/L)	LC_{50} (mg/L)	Author(s) (year)
Freshwater Organisms				
Water flea *Daphnia magna*	240	---	4068	Cowgill & Milazzo, 1991
Water flea *Ceriodaphnia dubia*	240	1866	6693	Cowgill & Milazzo, 1991
Water flea *Daphnia magna*	48	8500	15,800	Sloof *et al*., 1983
Water flea *Daphnia pulex*	48	5800	8800	Canton & Adema, 1978
Water flea *Daphnia cucullata*	48	---	7635	Canton & Adema, 1978
Snail *Planorbella trivolvis*	96	≥ 100	---	Ewell *et al*., 1986
Aquatic earthworm *Lumbriculus variegatus*	96	≥ 100	---	Ewell *et al*., 1986
Sideswimmer *Gammarus fasciatus*	96	≥ 100	---	Ewell *et al*., 1986
Pillbug *Caecidotea intermedia*	96	≥ 100	---	Ewell *et al*., 1986
Flatworm *Dugesia dorotocephala*	96	≥ 100	---	Ewell *et al*., 1986
Marine Organism				
Harpacticoids *Nitocra spinipes*	96	---	16,700	Lindén *et al.*, 1979
King crab *Lithodes antarcticus*	168	750	---	Lombardo *et al*., 1991
Grass shrimp *Palaemonetes pugio*	288	---	69,400	Rayburn & Fisher, 1997
Brine shrimp *Artemia salina*	24	---	2100	Price *et al*., 1974

Table 13
Acute toxicity of acetone to aquatic vertebrates

Species	Duration (hr)	NOEC (mg/L)	LC_{50} (mg/L)	Author(s) (year)
Freshwater Fish				
Fathead minnow *Pimephales promelas*	48	12,000	15,000	Sloof *et al*., 1983
Fathead minnow *Pimephales promelas*	96	---	9100	Cardwell *et al*., 1974
Japanese medaka *Oryzias latipes*	48	9500	14,300	Sloof *et al*., 1983
Mosquito fish *Gambusia affinis*	96	10,000	13,000	Wallen *et al*., 1957
Goldfish *Carassius auratus*	24	5000	---	Bridié *et al.*, 1979
Brook trout *Salvelinus fontinalis*	96	---	6070	Cardwell *et al*., 1974
Golden Orfe *Leuciscus idus*	48	---	9880	Juhnke & Lüdemann, 1978
Bluegill sunfish *Lepomis macrochirus*	96	3700	8300	Cairns & Scheier, 1968
Rainbow trout *Salmo gairdnerii*	48	5700	7400	Sloof *et al*., 1983
Bleak *Alburnus alburnus*	96	---	11,000	Lindén *et al.*, 1979
Guppy *Poecilia reticulata*	48	6700	9600	Sloof *et al*., 1983
Hydra *Hydra oligactis*	48	11,500	13,500	Sloof *et al*., 1983
Pond snail *Lymnaea stagnalis*	48	3500	7000	Sloof *et al*., 1983
Freshwater Amphibians				
Mexican axolotl *Ambystoma mexicanum*	48	12,000	20,000	Sloof & Baerselman, 1980
African clawed toad *Xenopus leavis*	48	20,000	24,000	Sloof & Baerselman, 1980
Insects				
Mosquito *Aedes aegypti*	48	3500	15,000	Sloof *et al*., 1983
Mosquito *Culex pipens*	48	8000	17,000	Sloof *et al*., 1983

3.2.3 *Other Effects*

The ability of acetone to inhibit cell multiplication has been examined in a wide variety of microorganisms (Table 14). The results have generally indicated mild to minimal toxicity with NOECs greater than 1700 mg/L for exposures lasting from 6 hr to 4 days. Longer exposure periods of 7 to 8 days with bacteria produced mixed results; but overall the data indicate a low degree of toxicity for acetone. The only exception to these findings were the results obtained with the flagellated protozoa (*Entosiphon sulcatum*) which yielded a 3-day NOEC of 28 mg/L. This was likely a spurious value, however, and the result could not be verified from the tests with other species of protozoa.

The four species of green algae examined in the multiplication inhibition test were relatively insensitive to the effects of acetone treatment. The lowest NOEC of 3400 mg/L was obtained following the 48-hr treatment of *Chlorella pyrenoidosa*. The lowest NOEC for bacteria, in contrast, was found to be 530 mg/L following the 192-hr treatment of *Microcystis aeruginosa*. The IC_{50} values for acetone have also been measured and compared using commercial and natural bacterial test cultures. The IC_{50} value of 48,000 mg/L obtained using the Polytox™ test system was found to compare favorably with the IC_{50} of 48,619 mg/L for an activated sludge test culture (Nirmalakhandan *et al*., 1994). The EC_{50} value for acetone in the Microtox™ test using the bacteria *Photobacterium phosphoreum* was found to be about 14,000 mg/L (Chen and Que Hee, 1995).

Table 14
Acetone toxicity thresholds in the cell multiplication inhibition test

Species	Duration (hr)	NOEC (mg/L)	Author(s) (year)
Flagellated protozoa *Entosiphon sulcatum*	72	28	Bringmann & Kühn, 1978
Bacteria *Microcystis aeruginosa*	192	530	Bringmann & Kühn, 1978
Bacteria *Pseudomonas putida*	16	1700	Bringmann & Kühn, 1977
Ciliated protozoa *Uronema parduczi*	20	1710	Bringmann & Kühn, 1980
Green algae *Chlorella pyrenoidosa*	48	3400	Sloof *et al*., 1983
Flagellated protozoa *Chilomonas paramecium*	48	3520	Bringmann & Kühn, 1980
Green algae *Scenedesmus pannonicus*	48	4740	Sloof *et al*., 1983
Marine diatom *Skeletonema costatum*	120	6000	Cowgill *et al*., 1989
Green algae *Selenastrum capricornutum*	96	7000	Sloof *et al*., 1983
Green algae *Scenedesmus quadricauda*	168	7500	Bringmann & Kühn, 1980
Freshwater diatom *Nitzschia linearis*	120	11,610	Patrick *et al*., 1968
Bacteria *Escherichia coli*	1.5	25,000	Reinhartz *et al*., 1987

3.3 Initial Assessment for the Environment

Considering the availability of acute data for algae, crustaceans, and fish an assessment factor of 100 was used to calculate a predicted no effect concentration (PNEC) for acetone in an aqueous environment. Using the LC_{50} value of 2100 mg/L obtained with the marine brine shrimp (*Artemia salina*), the lowest PNEC value for acetone was calculated to be 21 mg/L.

The lowest PNEC was compared to the $PEC_{(local)}$ and $PEC_{(global)}$ values for water (Table 11) to calculate PEC/PNEC ratios. The $PEC_{(global)}$ of 50 µg/L produced a PEC/PNEC

ratio of 0.002; whereas, the $PEC_{(local)}$ value of 2500 μg/L yielded a ratio of 0.12. These margins of exposure are each less than one; acetone was therefore judged to have low environmental risk potential.

4. HUMAN HEALTH

4.1 Human Exposure

Virtually every organ and tissue within the human body contains some acetone, which is one of three biochemicals collectively referred to as ketone bodies. Measurable amounts of acetone are continuously being excreted in the breath and urine of humans as a result of its high volatility and solubility in water (Brega *et al*., 1991). The acetone found in the body is produced in the liver following the utilization of stored fats and lipids as a source of energy (Landau and Brunengraber, 1987). The ability of humans to naturally produce and dispose of acetone may to a large degree explain its relatively low toxicity following external exposure to moderate amounts of the vapor or liquid (Wigaeus *et al*., 1981; Haggard *et al*., 1944). The background levels of acetone in blood and urine can vary widely but tend to average 1 to 2 mg/L. The levels in expired alveolar air are, however, about 1000-fold lower at 1 μg/L (Morgott, 1993).

Exogenous exposures to acetone typically occur by the pulmonary route. The high blood- to-air partition coefficient suggests that a large percentage of inhaled acetone will be absorbed into the body; the occurrence, however, of a peculiar wash-in/wash-out effect effectively reduces the uptake to about 50% (Johanson, 1991). The miscibility of acetone in the fluid layers lining the lung appears to be responsible for the wash-in/wash-out phenomenon. Under normal conditions acetone is efficiently and effectively metabolized to a variety of products that are used as building blocks for the synthesis of glucose, amino acids, and other more complex biochemicals (Argilés, 1986). Sustained high blood levels of acetone can result in the induction of enzymes responsible for its own metabolism and the metabolism of other chemicals (Koop and Casazza, 1985; Forkert *et al*., 1994). This compensatory response to high blood levels is responsible for the ability of acetone to potentiate the hepato- and nephrotoxicity of chemicals that undergo metabolic activation by microsomal enzymes to form toxic metabolites.

4.1.1 *Occupational Exposure*

High airborne concentrations of acetone have been found in a variety of occupational environments (Table 15). These levels reflect the high volatility and low intrinsic toxicity which combine to make acetone an attractive industrial process solvent. The predominant route of both occupational and consumer exposure to acetone is through vapor inhalation. Oral and dermal uptake can occur, but the body burden from these exposure routes is relatively small compared to respiratory absorption. Impermeable gloves should be worn together with a supplied air respirator when working with liquid acetone or when the vapor concentration exceeds the occupational exposure limit.

Table 15
Exposure to acetone in various occupations

Factory Type	8-Hour TWA Concentration (mg/m^3)	Author(s) (year)
automotive repair shop	12 - 77	Winder & Turner, 1993
print shop	6 - 235	Nasterlack *et al*., 1994
electronics plant	2 - 648	Hallock *et al*., 1993
fiberglass fabrication	40 - 1580	DeRosa *et al.*, 1996
varnish production	5 - 1448	Franco *et al*., 1986
cellulose acetate factory	12 - 2876	Satoh *et al*., 1996

The estimated human exposure (EHE) value for workplace employees has been set at 1780 mg/m^3 based on an examination of the data in Table 15. This exposure value for acetone also agrees well with the occupational exposure limits established in many countries and provides some assurance that it represents a plausible worst case concentration.

4.1.2 C*onsumer Exposure*

Acetone can be found in wide variety of consumer and commercial products but only a few are known to contain high concentrations (Sack *et al*., 1992). These include paints and paint-related products, such as paint thinners, finger nail polish removers, automotive waxes and tar removers (Table 16). Consumer exposures will most likely occur by the inhalation route and will be the greatest for those using adhesives, automotive products, and paint-related products that contain a high percentage of acetone.

Table 16
Average acetone concentration in various consumer product categories

Product Category	Number Products Assayed	Product Prevalence (%)	Average Concentration (%)
oils, greases & lubricants	71	5.3	0.2
cleaners for electronic equipment	111	16.1	0.3
household cleaners & polishers	463	10.8	0.3
miscellaneous products	76	17.2	7.4
fabric & leather treatments	91	14.6	12.9
adhesive-related products	69	24.3	18.8
automotive products	111	22.7	28.1
paint-related products	167	51.5	29.3

Using a USEPA modelling program entitled SCIES (Screening Consumers Inhalation Exposure Software), a 45-min exposure model was created for the application of a spray contact adhesive that contained 21% acetone. This scenario was selected because it depicts a realistic short duration exposure that involves the direct indoor air release of

large amounts of acetone. Although consumer products such as nail polish removers can contain 70 to 80% acetone, the resulting air acetone concentrations are generally lower than those described in the following scenario because of the small volumes of liquid typically applied. The spray contact adhesive scenario describes a plausible worst case consumer application where respirators would not be worn because of the short task duration and relatively low VOC content of the product.

SPRAY CONTACT ADHESIVE SCENARIO

Input Parameters

Use Rate	:	1 event/year
Mass of Product	:	225.0 g
Duration of Use	:	0.66 hr
Zone 1 Volume	:	40.0 m^3
Whole House Volume	:	292.0 m^3
House Air Exchange Rate	:	0.20 room air exchanges/hr
User Inhalation Rate	:	1.20 m^3/hr (during use)
User Inhalation Rate	:	1.10 m^3/hr (after use)
Molecular Weight	:	58.08 g/mole
Vapor Pressure	:	182 torr
Weight Fraction	:	0.210
Starting Time	:	9:00 AM

Output Summary

Evaporation Time	:	0.021 hr
Release Time	:	0.66 hr (duration of exposure)
Duration Following Use	:	8759.34 hr
Interval Between Uses	:	8760.00 hr

User Potential Dose Rate From Inhalation	:	1264.3 mg/yr
Non-User Potential Dose Rate From Inhalation	:	561.6 mg/yr

	Average (mg/m^3)	Peak (mg/m^3)
Concentration in Zone of Release :		
During period of use	556.03	907.19
During period after use	0.18	847.86
Concentration in Zone 2 :		
During period of use	10.90	27.75
During period after use	0.07	82.90
User and Non-User Exposure Concentration :		
Person using product (user)	0.13	907.19
Person not using product (non-user)	0.06	82.90

The modelling results shown above indicate average and peak exposures to acetone of 556 and 907 mg/m^3, respectively. The estimated short-term human exposure (EHE)

value associated with the use of consumer products was therefore set at the peak exposure concentration of 900 mg/m^3 that was predicted in this scenario.

4.1.3 *Indirect Exposure*

Acetone levels in the body at any point in time are reflective of free fatty acid utilization and acetoacetate production by the liver. Consequently, many normal and abnormal physiological states can appreciably increase the body burden of acetone through the process of ketogenesis. Children and adolescents typically have higher acetone blood levels than adults due to their higher energy expenditure. In fact, 2 to 5 day old infants have been found to have acetone blood levels ranging as high as 140 mg/L (Peden, 1964). Furthermore, vigorous exercise and the resulting utilization of fatty acids as a fuel source can lead to a condition commonly called post-exercise ketosis that results in a dramatic increase in blood ketone body concentrations. In addition to these normal physiological conditions, there are a number of clinical states that can result in human ketosis. In each of these conditions, the ketosis can be traced to the increased mobilization and utilization of free fatty acids by the liver. These conditions include pregnancy, fasting, prolonged vomiting, and alcoholism (Morgott, 1993).

Other clinical conditions, such as diabetic ketoacidosis and starvation, can lead to much larger increases in blood acetone levels (Table 17). In each of these situations, the elevations in blood acetone are typically accompanied by even larger increases in the remaining two ketone bodies, acetoacetate and β-hydroxybutyrate (Sulway *et al*., 1971). Unlike acetone, however, these two ketone bodies disrupt normal acid-base balance and cause many of the acute symptoms of diabetes due to their ionization (Winek, 1976). Acetone, in contrast, is non-ionic and is produced together with carbonic acid during the breakdown of acetoacetate (Koorevaar and Van Stekelenburg, 1976). Because acetone has a normal physiological role in the body, the estimated short-term human exposure (EHE) value for endogenous acetone was set at 10 mg/L, which represents the upper limit for blood acetone in healthy individuals.

Table 17
Human plasma acetone concentrations expected under various exposure and health conditions

Physiological State or Condition	Plasma Concentration Range		
	(mg/L)	(mg %)	(mM)
healthy	< 10	< 1.0	< 0.17
occupational exposure	< 100	< 10.0	< 1.72
diabetic ketoacidosis	100 - 700	10.0 - 70.0	1.72 - 12.04
toxic exposure	> 200	> 20.0	> 3.44

4.2 Effects on Human Health

About twenty separate instances of human acetone poisoning have been reported in the medical literature. Many of these case reports have involved patients seen in hospital emergency wards following either accidental or intentional ingestion of acetone. The case reports provide a clear picture of the signs, symptoms, and prognosis that accompany acute acetone intoxication. The most noticeable features of high exposures to acetone vapor are irritation to the eyes, nose, and throat. If the exposure is extremely large, as in cases of accidental ingestion of liquid acetone, fatigue, irritability, dizziness, and breathing irregularities may occur. When the poisoning is severe, these symptoms may precede the development of gastrointestinal disturbances and a temporary loss of consciousness. While many reports of severe acetone poisoning have been reported in the literature, no deaths have ever been recorded.

The following three methods have been used to study the sensory irritation potential of acetone for the eyes, nose, and throat: physiological techniques, psychophysical methods, and subjective questionnaires. It is important to understand the differences between sensory irritation and both sensitization and chemical irritation. Sensory irritation, known also as the "common chemical sense" or chemesthesis, occurs when a vapor or gas interacts with trigeminal nerve receptors in the ocular or nasal mucosa. Sensory irritation often occurs as a physical sensation that is described using a variety of terms including: pungency, piquancy, stinging, burning, and tickling. Sensitization, in contrast, is an allergic reaction that is manifested through a either a cell-mediated (dermal sensitization) or a humoral response (pulmonary sensitization) by the immune system. Chemical or primary irritation denotes an inflammatory reaction with localized redness and swelling. This type of irritation is found when a chemical solid or liquid makes direct contact with the skin or eyes. Sensory irritation is a generally milder effect than either sensitization or chemical irritation.

The studies listed in Table 18 were conducted both in the workplace using acetone-exposed employees and in the laboratory using naive volunteers exposed to acetone in an inhalation chamber. The studies using objective physiological and psychophysical techniques showed acetone to be an extremely weak sensory irritant. Subjective symptom questionnaires, in contrast, indicated that acetone was a sensory irritant at much lower vapor concentrations. Recent research indicates that the irritancy responses observed using subjective symptom questionnaires are likely caused by the odor of acetone (Dalton *et al*., 1997). Investigators have shown that both acetone and phenyl ethyl alcohol, a known non-irritant with a strong odor, produced subjective irritancy responses in humans following a 20-min inhalation exposure at 1900 mg/m^3. Objective psychophysical methods, in contrast, showed little if any irritancy effect in humans exposed under the same conditions.

The scientific literature contains eight different studies that have measured either the neurobehavioral performance or neurophysiological response of humans exposed to acetone. Many of the early neurotoxicity studies with acetone were not amenable to reliable statistical analysis because of the variability in the data and the inability to

reproduce the results. A close inspection of these early investigations also reveals many problems with design, conduct, or interpretation that hinder their use.

Among more recent studies with acetone, NOAELs ranging from vapor concentrations of 600 mg/m^3 to greater than 2375 mg/m^3 have been reported. The wide range in effect levels are likely due to statistical errors caused by large numbers of independent variables, analytical problems, and the failure to use multiple concentrations to evaluate dose-response characteristics. Neurobehavioral studies with acetone-exposed employees have recently shown that 8-hr exposures up to 2375 mg/m^3 were not associated with any dose-related changes in reaction time, vigilance, or digit span scores (Satoh *et al*., 1996). When the test subjects were divided into three age groups, a statistically significant decrease in simple reaction time and digit span scores was observed in one of the groups 30 to 44 years of age, but not in the older or younger age groups.

Table 18
Reported cases of human sensory irritation from acetone vapors

Test Method	Type of Subjects	No Effect Level (mg/m^3)	Author(s) (year)
Subjective			
questionnaire	naive	475	Nelson *et al*., 1943
questionnaire	workers	< 595	Satoh *et al.*, 1996
questionnaire	naive	595	Matsushita *et al*., 1969
questionnaire	naive	1185	DiVincenzo *et al*., 1973
questionnaire	workers	1900	Raleigh & McGee, 1972
questionnaire	both	2375	Seeber *et al*., 1992
questionnaire	naive	2850	Stewart *et al*., 1975
questionnaire	workers	3560	Oglesby *et al*., 1949
Objective			
acoustic rhinometry	naive	7120	Roberts *et al*., 1996
spirometry	naive	18,985	Douglas, 1974)
psychophysics	naive	> 23,730	Cometto-Muñiz *et al*., 1993
psychophysics	naive	> 23,730	Cometto-Muñiz *et al*., 1995
laterialization	workers	> 35,600	Wysocki *et al*., 1997
laterialization	naive	> 83,070	Wysocki *et al*., 1997

The acute effects of a single exposure to acetone vapor have been examined in mice, rats, guinea pigs, and cats. The adverse effects observed in laboratory animals are generally similar to the signs of central nervous system depression seen in cases of human intoxication. Vapor concentrations in excess of 24,000 mg/m^3 are generally required to elicit any sign of acute acetone intoxication in laboratory animals. Animal studies have demonstrated that the acute narcotic effects of acetone are strongly dependent upon both the length and magnitude of the exposure (Flury and Wirth, 1934; Haggard *et al*., 1944; Kagen, 1924; Specht *et al*., 1939). Regardless of the species examined, the narcotic effects of acetone tend to proceed through several distinct phases that can be described as

follows: drowsiness, lack of coordination, loss of autonomic reflexes, narcosis, respiratory failure, and death.

The hallmark of animal studies with acetone is the extremely high vapor concentrations or long exposure duration needed to produce an adverse effect. An 8-hr inhalation LC_{50} value of 50,100 mg/m^3 was reported for female rats (Pozzani *et al*., 1959). Single-dose oral lethality studies have also been performed in rats, mice, and rabbits. The oral LD_{50} was found to be 10.7 mL/kg (8.5 g/kg) in rats, 90.4 mmol/kg (5.25 g/kg) in mice, and greater than 5.3 g/kg in rabbits (Smyth *et al*., 1962; Tanii *et al*., 1986; Krasavage *et al*., 1982). An examination of the oral LD_{50} values for male and female rats from different age groups reveals that acetone is more acutely toxic for newborn rats than for adults (Table 19). The LD_{50} values for rats aged 14 days and older were not, however, substantially different (Kimura *et al*., 1971).

Table 19
Acute lethality of acetone to Sprague-Dawley rats from different age groups

Age Group	Weight Range (g)	LD_{50} (g/kg)	95% Confidence Limits (g/kg)
newborn (24-48 hr)	5 - 8	2.8	2.1 - 4.8
immature (14 day)	16 - 50	7.1	4.9 - 10.1
young adult	80 - 160	11.5	8.6 - 15.3
old adult	300 - 470	10.7	9.8 - 11.8

The ability of acetone to dehydrate and delipidate unprotected skin is well known from industrial and laboratory experience. Laboratory animal studies have confirmed this observation and also shown a low potential for systemic toxicity following exposure by the dermal route. The 24-hr dermal LD_{50} was found to be greater than 20 mL/kg (15.7 g/kg) in rabbits (Smyth *et al*., 1969). Acetone did not cause contact hypersensitization in the mouse ear swelling test or the guinea pig maximization test (Descotes, 1988; Nakamura *et al*., 1994). The sensory irritation potential for acetone vapors was determined by measuring the concentration-related decline in the respiration rate of mice. The RD_{50} values for acetone were found to be 183,970 mg/m^3 and 55,725 mg/m^3 in two separate studies (Kane *et al*., 1980; De Ceaurriz *et al*., 1981).

Studies conducted in rabbits have generally shown that acetone can be a severe eye irritant when applied undiluted and left in contact with the cornea. Dilute aqueous solutions, however, are minimally irritating. Corneal thickness measurements three days after the treatment of rabbits with 0.1 mL of undiluted acetone produced severe eye irritation (Morgan *et al*., 1987). An acetone concentration of 3.9 M (225 g/L) was found to cause a 50% increase in ocular edema after a 1-hr exposure. Acetone treatment for up to several minutes was shown to destroy the corneal epithelium, but not the corneal stroma. All injury to the corneal epithelium was reversible within 4 to 6 days. Acetone was not found to be a corrosive eye irritant (Märtins *et al*., 1992).

The subchronic toxicity of acetone has been examined in rats following oral gavage and drinking water consumption. In the gavage study, acetone was administered in water to male and female rats for 90 consecutive days at dose levels of 100, 500, and 2500 mg/kg (Mayhew and Morrow, 1988). The rats showed an increase in several hematological parameters and an increase in the serum activity of three enzymes. Increases in the absolute liver and kidney weight were observed for female rats at the two highest dose levels. Increases in organ-to-body weight ratios were also observed, but only at the highest dose level tested. Male rats administered 2500 mg/kg showed an increase in organ-to-body weight ratios for the liver and kidney, but the absolute weights of the organs were unaffected. No liver pathology was observed, however some histopatho-logical abnormalities were observed in the renal tubular cells of male and female rats treated at the high dose.

In a more relevant study, acetone was administered in the drinking water of mice and rats for either 14 days or 13 weeks. The drinking water concentrations and calculated average daily doses of acetone are presented in Table 20 (Dietz *et al*., 1991). No mouse or rat mortality was observed in either the 14-day or the 13-week study. Overt clinical signs of toxicity were only observed in the rats treated at the 10% level in the 14-day study. Acetone-induced increases in relative kidney weight were observed in the male and female rats treated for 13 weeks. The kidney weight changes were reportedly associated with a nephropathy that occurred spontaneously in untreated control rats. The increases in the relative liver weight of male and female rats were not associated with histopatho-logic changes and may have been caused by microsomal enzyme induction. Hematologic effects consistent with macrocytic anemia were noted in male rats along with hyperpig-mentation in the spleen. The most notable findings in mice were increased liver and decreased spleen weights, which were confined exclusively to female mice administered a 5% concentration of acetone (Dietz, 1991). The authors concluded that the no-observed-effect-level was 1% for male rats and male mice, 2% for female mice, and 5% for female rats.

Table 20
Time-weighted-average dose for male and female Fisher 344 rats and B6C3/F_1 mice exposed to acetone in their drinking water

Water Concentration (%)	14-Day Average Dose (mg/kg/day)				13-Week Average Dose (mg/kg/day)			
	Rats		Mice		Rats		Mice	
	male	female	male	female	male	female	male	female
0.125	-	-	-	-	-	-	380	-
0.25	-	-	-	-	200	200	611	892
0.5	714	751	965	1569	400	600	1353	2007
1.0	1616	1485	1579	3023	900	1200	2258	4156
2.0	2559	2328	3896	5481	1700	1600	4858	5945
5.0	4312	4350	6348	8804	3400	3100	-	11,298
10.0	6942	8560	10,314	12,725	-	-	-	-

Acetone showed minimal reproductive and developmental effects in animals exposed either by inhalation or via drinking water. No reproductive performance changes or testicular histopathological effects were noted in male rats treated with 0.5% acetone in

their drinking water for 6 weeks (Larsen *et al*., 1991). In another study, however, an acetone drinking water concentration of 5% caused a mild decrease in testicular weight, a moderate increase in the incidence of abnormal sperm, and depressed sperm motility after 13 weeks of treatment (Dietz *et al*., 1991). These findings indicate that high concentrations of acetone can have a mild effect on rat spermatogenesis.

The potential for acetone vapors to cause developmental effects was examined in virgin and pregnant rats and mice (Mast *et al*., 1988). Mated rats were exposed by inhalation to 1045, 5220, or 26110 mg/m^3 of acetone on days 6 through 19 of gestation. Mice were ex-posed at concentrations of 1045, 5220, or 15665 mg/m^3 of acetone on days 6 through 17 of gestation. No effects were seen in the mean liver or kidney weights of pregnant dams, the organ-to-body weight ratios, the number of implantations, the mean percentage of live pups per litter, the mean percentage of resorptions per litter, or the fetal sex ratio. No treatment-related effects were seen in maternal or virgin body weight, or the maternal uterine weight of the treated mice. A treatment-related increase was observed in the liver-to-body weight ratios for pregnant dams. A statistically significant reduction in fetal weight, and a slight, but statistically significant increase in the incidence of late resorptions was also seen in mice exposed to 15,665 mg/m^3 of acetone. The incidence of fetal malformations in mice was not altered by gestational exposure to acetone at any exposure concentration. The no-observed-effect level for developmental toxicity was found to be 5220 mg/m^3 for both rats and mice. Acetone did not produce any teratogenic effects at any of the exposure concentrations tested. The no-observed-effect level for teratogenicity was, therefore, greater than or equal to 15,665 mg/m^3 for mice and 26,110 mg/m^3 for rats.

Mild neurobehavioral changes have been observed in rats repeatedly exposed to high vapor concentrations of acetone. Female rats were exposed 4 hr/day for 2 weeks at acetone concentrations of 7120, 14240, 28480, and 37975 mg/m^3 were examined for their response to avoidance and escape stimuli before and after each exposure (Goldberg *et al*., 1964). Repeated daily exposures to 14,240 mg/m^3 of acetone produced an inhibition of avoidance behavior but did not produce any signs of motor imbalance. Acetone concentrations of 28,480 and 37,975 mg/m^3 produced ataxia in several animals after a single exposure, however, a rapid tolerance developed and ataxia was not seen on subsequent days. In a recent schedule controlled operant performance study, acetone did not cause any permanent effects in rats exposed to the vapor for 13 weeks at 2375, 4750, and 9495 mg/m^3 (Christoph and Stadler, 1997).

Information on the carcinogenicity of acetone is available from dermal studies performed in mice. In each of these studies, acetone was used as the vehicle to evaluate the effects of a test chemical. The test design therefore included untreated and vehicle-treated study groups. The carcinogenicity of acetone was evaluated in a group of 29 female ICR/Ha Swiss mice treated topically with 0.1 mL of acetone or 0.1 mL of an acetone-water mixture (9:1) three times per week for up to 424 days (Van Duuren *et al*., 1978). Histopathological analysis of all major organs revealed a total of 14 lung tumors, one liver tumor, one forestomach tumor, and no skin tumors in the acetone and acetone/water treatment groups. Lung papillary tumors were seen in 37% of the untreated mice and 24% of the acetone or acetone-water treated mice. The incidence of forestomach tumors

in acetone or acetone-water treated mice was comparable to untreated mice. Except for one undifferentiated malignant liver tumor, which was not cited as a remarkable finding, the incidence of systemic tumors in the acetone and acetone-water treated mice was not different from the background incidence in untreated mice. In another study, the application of 0.2 mL of acetone to the shaved dorsal skin of male and female CF1 mice once per week for two years had no effect on the survival of the 300 animals tested (Zakova *et al*., 1985). Dermal inflammatory reactions (focal acanthosis, dermal fibrosis) were seen in 6% of the animals and a fibrosarcoma was seen in one male mouse. An historical analysis of the organ pathology observed in two previous dermal carcinogenicity studies showed no evidence of a treatment-related increase in tumors or organ lesions from acetone (Ward *et al*., 1986). Sixty female SENCAR mice received 0.2 mL of acetone once or twice per week for up to 92 weeks. The major organs and tissues from all of the animals were examined both macroscopically and microscopically following necropsy. Fifty percent of the animals survived past 96 weeks of age with 15 of the mice dying due to neoplastic lesions and 27 due to non-neoplastic lesions.

Acetone has been repeatedly tested in a variety of prokaryotic and eukaryotic test systems without causing genotoxic effects. Studies in the *Salmonella* assay have shown acetone to be non-mutagenic and to be an acceptable vehicle for dissolving and delivering water- insoluble chemicals to the tester strains (Anderson and MacGregor, 1980). EPA-spon-sored studies have shown acetone to be negative in *Salmonella* strains TA97, TA98, TA100, and TA1535 at levels up to 1 mg/plate (NTP, 1987). Subsequent studies then found that acetone was negative in strains TA92, TA94, TA98, TA100, TA1535, and TA1537 at a concentration of 10 mg/plate (Ishidate *et al*., 1984). Acetone was not geno-toxic to *Schizosaccharomyces pombe* either with or without metabolic activation (Abbondandolo *et al*., 1980). Acetone induced aneuploidy, but not mitotic recombination or point mutations, in *Saccharomyces cerevisiae* when tested at concentrations greater than 40 mg/mL using a cold-interruption procedure (Zimmermann *et al*., 1985). These effects were not observed, however, when *Saccharomyces cerevisiae* was tested according to the standard overnight incubation procedure (Albertini, 1991).

Acetone did not produce genotoxic effects in an embryo cell transformation assay performed in rats and mice, and was also negative in a micronucleus assay using hamsters (Rhim *et al*., 1974; Basler, 1986). Acetone did not cause chromosomal aberrations or sister chromatid exchanges in Chinese hamster ovary cells treated at concentrations up to 5 mg/mL (Loveday *et al*., 1990). Acetone concentrations ranging from 10.5 to 20.9 mM (0.6 to 1.2 mg/mL) also did not cause chromosomal aberrations or sister chromatid exchanges in cultured human lymphocytes (Norppa, 1981). Acetone did not cause point mutations at the thymidine kinase locus in L5178Y mouse lymphoma cells treated at a level of 10 mg/mL (Amacher *et al*., 1980).

An epidemiological evaluation of mortality and clinical laboratory data for 948 employees in a fiber production plant exposed to 8-hr average acetone concentrations of 900, 1830, and 2540 mg/m^3 over 23 years produced no unusual findings (Table 21). The liver enzymes, clinical chemistry values, and hematological parameters were all within normal range (Ott *et al*., 1983a,b,c). Standard mortality ratios for death from all causes, cardio-

vascular disease, and malignant neoplasms were below expectations by 55%, 61%, and 43%, respectively.

Table 21
Observed and expected mortality rates for men and women occupationally exposed to acetone

Cause of Death	Male Mortality Ratio		Female Mortality Ratio	
	observed	expected	observed	expected
all causes	24	53.8	3	6.7
malignant neoplasm	5	10.0	2	2.3
cardiovascular disease	15	40.4	2	2.8

Four health surveillance studies have been conducted on acetone-exposed employees from cellulose acetate facilities located worldwide. The studies did not reveal any evidence of systemic toxicity or dose-related adverse heath effects based on the results obtained from a wide variety of biochemical and hematological tests (Table 22).

Table 22
Occupational health surveys with acetone exposed workers

Factory Location	Number Examined	Employed (years)	Exposure (mg/m^3)	Clinical Measurements	Author (year)
United States	800	unknown	1425 - 5100	hematology & urinalysis	Oglesby *et al*., 1949
United States	948	< 23	900 - 2540	hematology, urinalysis, & mortality	Ott *et al*., 1983
Italy	60	> 5	1305 - 2490	hematology, urinalysis, & clinical chemistry	Grampella *et al*., 1987
Japan	110	15	48 - 2415	hematology, immunology, & clinical chemistry	Satoh *et al.*, 1996

4.3 Initial Assessment for Human Health

The inhalation EHE values for occupational and consumer groups have been set at 1780 and 900 mg/m^3, respectively. The indirect EHE level of 10 mg/L is based on the upper normal limit for acetone in the blood of a healthy adult human. The most critical effect of acetone inhalation for both industrial and consumer contact is central nervous system depression. This endpoint was selected over the more commonly reported sensory irritation effects based on the findings from a recently completed comprehensive review of the odor and irritancy potential of acetone (Arts *et al*., 1998). The authors of this review concluded that subjective reports of acetone's irritancy were unreliable and likely related its distinctive odor. Furthermore, the authors determined that the true irritancy threshold for acetone vapors was very high, ranging somewhere between 23,730 and 94,930 mg/m^3. Clinical case studies, controlled human volunteer studies, animal research, and occupational field evaluations all indicate that the NOAEL for the CNS-

related effects of acetone is about 2375 mg/m^3. The EHE/NOAEL ratio for these neurological effects indicate a margin of exposure of 0.75 for occupational use and 0.40 for the consumer use. Acetone is therefore considered to have a low potential for neurological risk to humans.

Using the following equation, the 900 mg/kg/day NOAEL observed in male rats from the subchronic drinking study may be used to calculate an equivalent human inhalation value for renal toxicity.

$$\text{Inhalation NOAEL}_{[\text{human}]} = \frac{\text{oral NOAEL}_{[\text{rat}]} \times 70\ \text{kg}}{\text{ventilation rate } (m^3/\text{d or h}) \times \text{uptake } (\%)}$$

Assuming a pulmonary uptake of 50%, a human ventilation rate of 21.6 m^3/day for consumer exposures and 10 m^3/8 hr for occupational exposures, the drinking water NOAEL was found to be equivalent to a 24-hr consumer inhalation value of 5833 mg/m^3 and an 8-hr occupational value of 12,600 mg/m^3. Using these NOAEL values, the EHE/NOAEL ratios indicate a margin of exposure of 0.15 for consumer contact and 0.14 for occupational exposure.

The NOAEL of 5220 mg/m^3 observed in both rats and the mice used in the developmental study was also used to calculate a human margin of exposure. The EHE/NOAEL ratio for developmental effects reveals a margin of exposure of 0.17 for the consumer use of acetone and 0.34 for occupational contact. Acetone is therefore considered to have a low potential for renal damage and developmental effects in humans.

The unconsciousness, respiratory distress, and vomiting associated with cases of accidental or intentional exposure to acetone appear to occur when the blood levels are excess of 1000 mg/L. Likewise, the drowsiness observed in patients with uncontrolled diabetes mellitus has been associated with acetone blood levels in excess of 150 mg/L. By comparison, an 8-hr occupational exposure to 1780 mg/m^3 of acetone is expected to result in an acetone blood level of about 60 mg/L. This shows that the blood levels associated with occupational exposures to acetone are far below those causing central nervous system depression.

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

An examination of all available information on the biological activity of acetone indicates that the vapors are mildly toxic after both direct contact or systemic absorption. The primary effect of acute high-level exposure appears to be central nervous system depres-sion. Comparative studies with other solvents have shown that the irritative properties of acetone vapor are extremely mild and are often confused with its odor. Although many cases of accidental or intentional human acetone poisoning have occurred, no instances of death or permanent injury have been recorded. Appreciable quantities of acetone are continually being produced and eliminated in the body as a

result of energy needs. Normal background levels in the blood can, therefore, dramatically fluctuate depending upon age, eating habits, and level of physical fitness.

The data indicate that acetone does not pose a neurotoxic, carcinogenic, or reproductive health hazard at the concentrations found anywhere in the environment. Information obtained from occupationally exposed individuals, animal feeding studies, and *in vitro* screening assays support this conclusion. The kidney appeared to be the most sensitive target tissue in both of these studies. Acetone has also been tested in a wide variety of aquatic and terrestrial organisms and produced minimal to mild effects in every instance. The mild effects have allowed acetone to be used as a carrier solvent for dissolving and testing less soluble chemicals. The preceding analysis shows that acetone has a low potential for harming both human health and the environment.

5.2 Recommendations

5.2.1 *Categories*

Acetone has a low priority for further work. The health and environmental effects of acetone have both been well studied.

References

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.

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

Amacher, D.E., Pailler, S.C., Turner, G.N., Ray, V.A., and Salsburg, D.S. (1980). Point mutations at the thymidine kinase locus in L5178Y mouse lymphoma cells. II. Test validation and interpretation. *Mutat. Res*. **72**,447-474.

Anderson, D. and MacGregor, D.B. (1980). The effect of solvents upon the yield of revertants in the *Salmonella*/activation mutagenicity assay. *Carcinogenesis* **1**,363-366.

Andersson, L. and Lundström, K. (1984). Milk and blood ketone bodies, blood isopropanol and plasma glucose in dairy cows; methodological studies and diurnal variations. *Zentralbl. Vet. Med. A* **31**,340-349.

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.

Argilés, J.M. (1986). Has acetone a role in the conversion of fat to carbohydrate in mammals? *Trends Biochem. Sci*. **11**,61-63.

Arnts, R.R. and Meeks, S.A. (1981). Biogenic hydrocarbon contribution to the ambient air of selected areas. *Atmos. Environ*. **15**,1643-1651.

Arts, J.H.E., Mojet, J., van Gemert, L.J., Emmen, H.H., Lammers, J.H.C.M., Marquart, J., Woutersen, R.A., and Feron, V.J. (1998). An analysis of human response to the irritancy of acetone vapours. TNO Report V98.357. TNO Nutrition and Food Research Institute. Zeist, The Netherlands.

Basler, A. (1986). Aneuploidy-inducing chemicals in yeast evaluated by the micronucleus test. *Mutat. Res*. **174**,11-13.

Betterton, E.A. (1991). The partitioning of ketones between the gas and aqueous phases. *Atmos. Environ*. **25A**,1473-1477.

Bhattacharya, S.K., Madura, R.L., Dobbs, R.A., Angara, R.V.R., and Tabak, H. (1996). Fate of selected RCRA compounds in a pilot-scale activated sludge system. *Water Environ. Res*. **68**,260-269.

Bizzari, S.N. (1996). CEH Marketing Research Report Acetone. Chemical Economics Handbook, SRI International. Menlo Park, CA.

Booher, L.E. and Janke, B. (1997). Air emissions from petroleum hydrocarbon fires during controlled burning. *Am. Ind. Hyg. Assoc. J*. **58**,359-365.

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.

Bridié, A.L., Wolff, C.J.M., and Winter, M. (1979). The acute toxicity of some petrochemicals to goldfish. *Water Res*. **13**,623-626.

Bringmann, G. and Kühn, R. (1980). Comparison of the toxicity thresholds of water pollutants to bacteria, algae, and protozoa in the cell multiplication inhibition test. *Water Res*. **14**,231-241.

Bringmann, G. and Kühn, R. (1978). Testing of substances for their toxicity threshold: Model organisms *Microcystis (Diplocystis) aeruginosa* and *Secenedesmus quadricauda. Mitt. Int. Verein. Limnol.* **21**,275-284.

Bringmann, G. and Kühn, R. (1977). Grenzwerte der Schadwirkung wassergefährdender Stoffe gegen Bakterien (*Pseudomonas putida*) und Grünalgen (*Scenedesmus quadricauda*) im Zellvermehrungshemmtest. *Z. Wasser Abwasser Forsch*. **10**,87-98 (German).

Brosseau, J. and Heitz, M. (1994). Trace gas compound emissions from municipal landfill sanitary sites. *Atmos. Environ*. **28**,285-293.

Brown, K.W. and Donnelly, K.C. (1988) An estimation of the risk associated with the organic constituents of hazardous and municipal waste landfill leachates. *Haz. Waste Haz. Mater*. **5**,1-30.

Cairns, J. and Scheier, A. (1968). A comparison of the toxicity of some common industrial waste components tested individually and combined. *Prog. Fish Culturist* **30**,3-8.

Canton, J.H. and Adema, D.M.M. (1978). Reproducibility 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.

Cardwell, R.D., Foreman, D.G., Payne, T.R., and Wilbur, D.J. (1974). Acute and chronic toxicity of four organic chemicals to fish. US Environmental Protection Agency, Envirogenics Contract 68-01-0711. Environmental Research Laboratory. Duluth, MN.

Cavanagh, L.A., Schadt, C.F., and Robinson, E. (1969). Atmospheric hydrocarbon and carbon monoxide measurements at Point Barrow, Alaska. *Environ. Sci. Technol*. **3**,251-257.

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.

Chen, H.-F. and Que Hee, S.S. (1995). Ketone EC_{50} values in the Microtox test. *Ecotoxicol. Environ. Safety* **30**,120-123.

Christoph, G.R., Keller, D.A., and Stadler, J.C. (1997). Subchronic inhalation of acetone vapor: Schedule-controlled operant behavior and time-course of blood acetone concentration in rats. *Toxicologist* **17**,63 (Abstract).

Collins, R.P. and Kalnins, K. (1966). Carbonyl compounds produced by *Cryptomonas ovata* var. *palustris. J. Protozool*. **13**,435-437.

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.

Cometto-Muñiz, J.E. and Cain, W.S. (1995). Relative sensitivity of the ocular trigeminal, nasal trigeminal and olfactory systems to airborne chemicals. *Chem. Senses* **20**,191-198.

Corwin, J.F. (1969). Volatile oxygen-containing organic compounds in sea water: Determination. *Bull. Marine Sci*. **19**,504-509.

Cowgill, U.M. and Milazzo, D.P. (1991). The sensitivity of *Ceriodaphnia dubia* and *Daphnia magna* to seven chemicals utilizing the three-brood test. *Arch. Environ. Contam. Toxicol*. **20**,211-217.

Cowgill, U.M., Milazzo, D.P., and Landenberger, B.D. (1991). The sensitivity of *Lemna gibba* G-3 and four clones of *Lemna minor* to eight common chemicals using a 7-day test. *J. Water Pollut. Control Fed*. **63**,991-998.

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.

Daisey, J.M., Hodgson, A.T., Fisk, W.J., Mendell, M.J., and Ten Brinke, J. (1994). Volatile organic compounds in twelve California office buildings: Classes, concentrations and sources. *Atmos. Environ*. **28**,3557-3562.

Dalton, P., Wysocki, C.J., Brody, M.J., and Lawley, H.J. (1997). Perceived odor, irritation and health symptoms following short-term exposure to acetone. *Am. J. Ind. Med*. **31**,558-569.

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.

Dechow, M., Sohn, H., and Steinhanses, J. (1997). Concentrations of selected contaminants in cabin air of Airbus aircrafts. *Chemosphere* **35**,21-31.

De Rosa, E., Cellini, M., Sessa, G., Scapellato, M.L., Marcuzzo, G., and Bartolucci, G.B. (1996). The importance of sampling time and co-exposure to acetone in the biological monitoring of styrene-exposed workers. *Appl. Occup. Environ. Hyg*. **11**,471-475.

Derwent, R.G., Jenkin, M.E., and Saunders, S.M. (1996). Photochemical ozone creation potentials for a large number of reactive hydrocarbons under European conditions. *Atmos. Environ*. **30**,181-199.

Descotes, J. (1988). Identification of contact allergens: The mouse ear sensitization assay. *J. Toxicol. Cut. Ocular Toxicol*. **7**,263-272.

Devos, M., Patte, F., Rouault, J., Laffort, P., and Van Gemert, L.J. (1990). In: *Standardized Human Olfactory Thresholds*, p. 145. Oxford University Press. Oxford, United Kingdom.

Dewalle, F.B. and Chian, E.S.K. (1981). Detection of trace organic's in well water near a solid waste landfill. *J. Am. Water Works Assoc*. **73**,206-211.

Dietz, D.D. (1991). Toxicity studies of acetone in F344/N rats and B6C3F1 mice (drinking water studies). US Dept. of Health Human Services Report, Report NIH 91-3122, pp. 1-38. National Toxicology Program. Research Triangle Park, NC.

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.

Di Vincenzo, 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.

Euler, D.E., Davé, S.J., and Guo, H. (1996). Effect of cigarette smoking on pentane excretion in alveolar breath. *Clin. Chem*. **42**,303-308.

Ewell, W.S., Gorsuch, J.W., Kringle, R.O., Robillard, K.A., and Spiegel, R.C. (1986). Simultaneous evaluation of the acute effects of chemicals on seven aquatic species. *Environ. Toxicol. Chem.* **5**,831-840.

Flury, F. and Wirth, W. (1934). Zur Toxikologie der Lösungsmittel (Verschiedene Ester, Aceton, Methylalkohol). *Arch. Gewerbepath. Gewerhyg*. **5**,1 (German).

Forkert, P.G., Redza, Z.M., Mangos, S., Park, S.S., and Tam, S.-P. (1994). Induction and regulation of CYP2E1 in murine liver after acute and chronic acetone administration. *Drug Metab. Dispos*. **22**,248-253.

Franco, G., Fonte, R., Tempini, G., and Candura, F. (1986). Serum bile acid concentrations as a liver function test in workers occupationally exposed to organic solvents. *Int. Arch. Occup. Environ. Health* **58**,157-164.

George, H.A., Johnson, J.L., Moore, W.E.C., Holdeman, L.V., and Chen, J.S. (1983). Acetone, isopropanol, and butanol production by *Clostridium beijerinckii* (syn. *Clostridium butylicium*) and *Clostridium aurantibutyricum. Appl. Environ. Microbiol*. **45**,1160-1163.

Goldan, P.D., Kuster, W.C., and Fehsenfeld, F.C. (1997). Nonmethane hydrocarbon measurements during the tropospheric OH photochemistry experiment. *J. Geophys. Res*. **102**,6315-6324.

Goldan, P.D., Trainer, M., Kuster, W.C., Parrish, D.D., Carpenter, J., Roberts, J.M., Yee, J.E., and Fehsenfeld, F.C. (1995). Measurements of hydrocarbons, oxygenated hydrocarbons carbon monoxide, and nitrogen oxides in an urban basin in Colorado: Implications for emissions inventories. *J. Geophys. Res*. **100**,22771-22783.

Goldberg, M.E., Johnson, H.E., Pozzanni, U.C., and Smythe, H.F. (1964). Effect of repeated inhalation of vapors of industrial solvents on animal behavior. I. Evaluation of nine solvent vapors on pole-climb performance in rats. *Am. Ind. Hyg. Assoc. J*. **25**,369-375.

Gorsuch, J.W., Kringle, R.O., and Robillard, K.A. (1990). Chemical effects on the germination and early growth of terrestrial plants. In: *Plants for Toxicity Assessment*, W. Wang, J.W. Gorsuch, and W.R. Lower, eds., pp. 49-58, ASTM STP 1091. American Society of Testing Materials. Philadelphia, PA.

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*. Wolfheze, Holland.

Granby, K., Christensen, C.S., and Lohse, C. (1997). Urban and semi-rural observations of carboxylic acids and carbonyls. *Atmos. Environ*. **31**,1403-1415.

Grimaldi, F., Bacle, D., Bouthiba, M., Gouezo, F., Viala, A., Casabianca, S., Muls, E., Figos, J., Esberard, N., and Masquelez, N. (1996). Study of air pollution by carbonyl compounds in automobile exhaust. *Pollut. Atmos*. **149**,68-76.

Grosjean, E., Grosjean, D., Fraser, M.P., and Cass, G.R. (1996). Air quality model evaluation data for organics. 2. C_1-C_{14} carbonyls in Los Angeles air. *Environ. Sci. Technol*. **30**,2687-2703.

Grosjean, D., Miguel, A.H., and Tavares, T.M. (1990). Urban air pollution in Brazil: Acetaldehyde and other carbonyls. *Atmos. Environ*. **24B**,101-106.

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.

Hallock, M.F., Hammond, K., Kenyon, E., Smith, T., and Smith, E. (1993). Assessment of task and peak exposures to solvents in the microelectronics fabrication industry. *Appl. Occup. Environ. Hyg*. **8**,945-954.

Hartstein, A.M. and Forshey, D.R. (1974). Coal mine combustion products. Neoprenes, polyvinyl chloride compositions, urethane foam, and wood. US Department of the Interior, Report 7977. Bureau of Mines. Pittsburgh, PA.

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.

Hill, E.F., Heath, R.G., Spann, J.W., and Williams, J.D. (1975). Lethal dietary toxicities of environmental pollutants to birds. US Department of the Interior, Wildlife Report No. 191. Fish and Wildlife Service. Washington, DC.

Hoshika, Y., Nihei, Y., and Muto, G. (1981). Pattern display for characterization of trace amounts of odorants discharged from nine odour sources. *Analyst* **106**,1187-1202.

Howard, P.H., Sage, G.W., Jarvis, W.F., and Gray, D.A. (1990). Acetone. In: *Handbook of Environmental Fate and Exposure Data for Organic Chemicals*, pp. 9-18. Lewis Publishers, Inc. New York, NY.

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.

Isidorov, V.A., Zenkevich, I.G., and Ioffe, B.V. (1985). Volatile organic compounds in the atmosphere of forests. *Atmos. Environ*. **19**,1-8.

Jarke, F.H., Dravnieks, A., and Gordon, S.M. (1981). Organic contaminants in indoor air and their relation to outdoor contaminants. *ASHRAE Trans*. **87**,153-166.

Johanson, G. (1991). Modelling of respiratory exchange of polar solvents. *Ann. Occup. Hyg.* **35**,323-339.

Jonsson, A., Persson, K.A., and Grigoriadis, V. (1985). Measurements of some low molecular-weight oxygenated, aromatic, and chlorinated hydrocarbons in ambient air and in vehicle emissions. *Environ. Int*. **11**,383-392.

Juhnke, I. and Luedemann, D. (1978). Ergebnisse der Untersuchung von 200 chemischen Verbindungen auf akute Fishtoxizität mit dem Goldorftest. *Z. Wasser Abwasser Forsch*. **11**,161-164 (German).

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.

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 (German).

Kalabokas, P., Hatzianestis, J., Bartzis, J., and Mimikos, N. (1997). Seasonal and diurnal variation of carbonyl compounds concentration levels in the atmosphere of the Athens basin. *Fresenius Environ. Bull*. **6**,172-177.

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

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.

Khalil, M.A.K. and Rasmussen, R.A. (1992). Forest hydrocarbon emissions: Relationships between fluxes and ambient concentrations. *J. Air Waste Manage. Assoc*. **42**,810-813.

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.

Koop, D.R. and Casazza, J.P. (1985). Identification of ethanol-inducible P-450 isozyme 3a as the acetone and acetol monooxygenase of rabbit microsomes. *J. Biol. Chem*. **260**,13607-13612.

Koorevaar, G. and Van Stekelenburg, G.J. (1976). Mammalian acetoacetate decarboxylase activity. Its distribution in subfractions of human albumin and occurrence in various tissues of the rat. *Clin. Chem. Acta* **71**,173-183.

Krasavage, W.J., O'Donoghue, J.L., and Di Vincenzo, G.D. (1982). Ketones. In: *Patty's Industrial Hygiene and Toxicology*, G.D. Clayton and F.E. Clayton, eds., 3rd ed., Vol. IIC, pp. 4720-4727. John Wiley & Sons, Inc. New York, NY.

Kristen, U., Kappler, R., and Van Aken, J.P. (1994). The pollen tube growth test (PTG-test). *Invittox Protocol* **55**,1-7.

Lamb, C.B. and Jenkins, G.F. (1952). BOD of synthetic organic chemicals. *Proc. Ind. Waste Conf*. **36**,326-339.

Landau, B.R. and Brunengraber, H. (1987). The role of acetone in the conversion of fat to carbohydrate. *Trends Biochem. Sci.* **12**,113-114.

Larsen, J.J., Lykkegaard, M., and Ladefoged, O. (1991). Infertility in rats induced by 2,5-hexanedione in combination with acetone. *Pharmacol. Toxicol*. **69**,43-46.

Le Blanc, 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.

Lee, Y.-N., Zhou, X., and Hallock, K. (1995). Atmospheric carbonyl compounds at a rural southeastern United States site. *J. Geophys. Res*. **100**,25933-25944.

Leonardos, G., Kendall, D., and Barnard, N. (1969). Odor threshold determinations of 53 odorant chemicals. *J. Air Poll. Control Assoc*. **19**,91-95.

Lewis, C.W. and Zweidinger, R.B. (1992). Apportionment of residential indoor aerosol VOC and aldehyde species to indoor and outdoor sources, and their source strengths. *Atmos. Environ*. **26A**,2179-2184.

Li, S.-M., Anlauf, K.G., Wiebe, H.A., Bottenheim,, J.W., Shepson, P.B., and Biesenthal, T. (1997). Emission rates and photochemical production efficiencies of nitrogen oxides, ketones, and aldehydes in the lower Fraser valley during the summer Pacific 1993 oxidant study. *Atmos. Environ.* **31**,2037-2048.

Lindén, E., Bengtsson, B.-E., Svanberg, O., and Sundström, G. (1979). The acute toxicity of 78 chemicals and pesticide formulations against two brackish water organisms, the bleak (*Alburnus alburnus*) and the harpacticoid (*Nitocra spinipes*). *Chemosphere* **8**,843-851.

Line, D.E., Wu, J., Arnold, J.A., Jennings, G.D., and Rubin, A.R. (1997). Water quality of first flush runoff from 20 industrial sites. *Water Environ. Res*. **69**,305-310.

Lipari, F., Dasch, J.M., and Scruggs, W.F. (1984). Aldehyde emissions from wood-burning fireplaces. *Environ. Sci. Technol*. **18**,326-330.

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.

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.

Mackay, D. and Paterson, S. (1981). Calculating fugacity. *Environ. Sci. Technol*. **15**,1006-1014.

Märtins, T., Pauluhn, J., and Machemer, L. (1992). Analysis of alternate methods for determining ocular irritation. *Food Chem. Toxicol*. **30**,1061-1067.

Mast, T.J., Evanoff, J.J., Rommereim, 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. National Institute of Environmental Health Sciences, National Toxicology Program,

Contract DE AC06-76RLO 1830. Pacific Northwest Laboratory, Battelle Memorial Institute. Richland, WA.

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 (Japanese).

Mayhew, D.A. and Morrow, L.D. (1988). Ninety day gavage study in albino rats using acetone. US Environmental Protection Agency, American Biogenics Corp., Contract No. 68-01-7075. Office of Solid Waste. Washington, DC.

Meylan, W.M. and Howard, P.H. (1998). User's guide for the ECOSAR class program. US Environmental Protection Agency, Health and Environmental Review Division. Washington, DC.

Meyrahn, H., Pauly, J., Schneider, W., and Warneck, P. (1986). Quantum yields for the photodissociation of acetone in air and an estimate for the life time of acetone in the lower troposphere. *J. Atmos. Chem*. **4**,277-291.

Morgan, R.L., Sorenson, S.S., and Castles, T.R. (1987). Prediction of ocular irritation by corneal pachymetry. *Food Chem. Toxicol*. **8**,609-613.

Morgott, D.A. (1993). Acetone. In: *Patty's Industrial Hygiene and Toxicology*, G.D. Clayton and F.E. Clayton, eds., 4th ed., Volume II, Part A, Chapter 5, pp. 149-281. John Wiley & Sons, Inc. New York, NY.

NTP (1987). Cellular and genetic toxicology. In: *National Toxicology Program Fiscal Year 1987 Annual Plan*, pp. 43-96. US Department of Health and Human Services, National Toxicology Program, Report No. NTP-87-001. National Institute of Environmental Health Sciences. Research Triangle Park, NC.

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.

Nasterlack, M., Triebig, G., and Stelzer, O. (1994). Hepatotoxic effects of solvent exposure around permissible limits and alcohol consumption in printers over a 4-year period. *Int. Arch. Occup. Environ. Health* **66**,161-165.

Nelson, K.W., Ege, 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.

Nirmalakhandan, N., Arulgnanendran, V., Mohsin, M., Sun, B., and Cadena, F. (1994). Toxicity of mixtures of organic chemicals to microorganisms. *Water Res*. **28**,543-551.

Norppa, H. (1981). The *in vitro* induction of sister chromatid exchanges and chromosome aberrations in human lymphocytes by styrene derivatives. *Carcinogenesis* **2**,237-242.

Oglesby, F.L., Williams, J.L., and Fassett, D.W. (1949). Eighteen-year experience with acetone. In: *American Industrial Hygiene Association Annual Meeting*. Detroit, MI.

Oser, B.L. and Ford, R.A. (1973). Recent progress in the consideration of flavoring ingredients under the Food Additives amendment. 6. GRAS substances. *Food Technol*. **27**,64-67.

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

Patrick, R. and Cairns, J. (1968). The relative sensitivity of diatoms, snails, and fish to twenty common constituents of industrial wastes. *Progr. Fish Culturist* **30**,137-140.

Peden, V.H. (1964). Determination of individual serum "ketone bodies," with normal values in infants and children. *J. Lab. Clin. Med*. **63**,332-343.

Platen, H. and Schink, B. (1989). Anaerobic degradation of acetone and higher ketones via carboxylation by newly isolated denitrifying bacteria. *J. Gen. Microbiol*. **135**,883-891.

Possanzini, M., Di Palo, V., Petricca, M., Fratarcangeli, R., and Brocco, D. (1996). Measurements of lower carbonyls in Rome ambient air. *Atmos. Environ*. **30**,3757-3764.

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.

Price, K.S., Waggy, G.T., and Conway, R.A. (1974). Brine shrimp bioassay and seawater BOD of petrochemicals. *J. Water Pollut. Control Fed*. **46**,63-77.

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.

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.

Rayburn, J.R. and Fisher, W.S. (1997). Developmental toxicity of three carrier solvents using embryos of the grass shrimp, *Palaemonetes pugio*. *Arch. Environ. Contam. Toxicol.* **33**,217-221.

Reinhartz, A., Lambert, 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.

Rhim, J.S., Park, D.K., Weisburger, E.K., and Weisburger, J.H. (1974). Evaluation of an *in vitro* assay system for carcinogens based on prior infection of rodent cells with nontransforming RNA tumor virus. *J. Natl. Cancer Inst*. **52**,1167-1173.

Roberts, D.N., MacGregor, F.B., Robson, A.G., Cocker, J., Rusznac, C., Schroter, R., Davies, R.J., and Pride, N.B. (1996). Monitoring of the nasal response to industrial and environmental

stimuli. In: *Society of Occupational Medicine Annual Scientific Meeting*. Birmingham, United Kingdom.

Rustung, E., Koren, F., and Föyen, A. (1931). Über Aufnahme und von Aceton im Organismus von Kaltblütern. *Biochem. Z.* **242**,366-376 (German).

Sabel, G.V. and Clark, T.P. (1984). Volatile organic compounds as indicators of municipal solid waste leachate contamination. *Waste Manage. Res*. **2**,119-130.

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.

Sanders, P.F. (1995). Calculation of soil cleanup criteria for volatile organic compounds as controlled by the soil-to-groundwater pathway: Comparison of four unsaturated soil zone leaching models. *J. Soil Contam*. **4**,1-24.

Satoh, T., Omae, K., Nakashima, H., Takebayashi, T., Matsumura, H., Kawai, T., Nakaza, M., and Sakurai, H. (1996). Relationship between acetone exposure concentration and health effects in acetate fiber plant workers. *Int. Arch. Occup. Environ. Health* **68**,147-153.

Schubert, U., Wisanowsky, L., and Kull, U. (1995). Determination of phytotoxicity of several volatile organic compounds by investigating the germination pattern of tobacco pollen. *J. Plant Physiol*. **145**,514-518.

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.

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.

Singh, H.B., Kanakidou, M., Crutzen, P.J., and Jacobs, D.J. (1995). High concentrations and photochemical fate of oxygenated hydrocarbons in the global troposphere. *Nature* **378**,50-54.

Slemr, J., Junkermann, W., and Volz-Thomas, A. (1996). Temporal variations in formaldehyde, acetaldehyde and acetone and budget of formaldehyde at a rural site in southern Germany. *Atmos. Environ*. **30**,3667-3676.

Slooff, W., Canton, J.H., and Hermens, J.L.M. (1983). Comparison of the susceptibility of 22 freshwater species to 15 chemical compounds. I. (Sub)acute toxicity tests. *Aquatic Toxicol*. **4**,113-128.

Slooff, W. and Baerselman, R. (1980). Comparison of the usefulness of the Mexican axolotl (*Ambystoma mexicanum*) and the clawed toad (*Xenopus laevis*) in toxicological bioassays. *Bull. Environ. Contam. Toxicol*. **14**,439-443.

Smith, M.S., Francis, A.J., and Duxbury, J.M. (1977). Collection and analysis of organic gases from natural ecosystems: Application to poultry manure. *Environ. Sci. Technol*. **11**,51-55.

Smyth, H.F., Weil, C.S., West, J.S., and Carpenter, C.P. (1969). An exploration of joint toxic action: Twenty-seven industrial chemicals intubated in rats in all possible pairs. *Toxicol. Appl. Pharmacol*. **14**,340-347.

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.

Solberg, S., Dye, C., Schmidbauer, N., Herzog, A., and Gehrig, R. (1996). Carbonyls and non-methane hydrocarbons at rural European sites from the Mediterranean to the Arctic. *J. Atmos. Chem*. **25**,33-66.

Specht, H., Miller, J.W., and Valaer, P.J. (1939). Acute response of guinea pigs to the inhalation of dimethyl ketone (acetone) vapor in air. *Pub. Health Rep*. **52**,944-954.

Spicer, C.W., Buxton, B.E., Holden, M.W., Smith, D.L., Kelly, T.J., Rust, S.W., Pate, A.D., Sverdrup, G.M., and Chuang, J.C. (1996). Variability of hazardous air pollutants in an urban area. *Atmos. Environ*. **30**,3443-3456.

Steinberg, S.P. and Kreamer, D.K. (1993). Evaluation of the sorption of volatile organic compounds by unsaturated calcareous soil from southwestern Nevada using inverse gas chromatography. *Environ. Sci. Technol*. **27**,883-888.

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. US Dept. of Commerce, Report No. PB82-172917. National Institute for Occupational Safety and Health. Cincinnati, OH.

Sulway, M.J., Trotter, M.D., Trotter, E., and Malins, J.M. (1971). Acetone in uncontrolled diabetes. *Postgrad. Med. J.* **47(Suppl)**,383-387.

Sunesson, A.-L., Nilsson, C.-A., Andersson, B., and Blomquist, G. (1966). Volatile metabolites produced by two fungal species cultivated on building materials. *Ann. Occup. Hyg*. **40**,397-410.

Tanii, H., Tsuji, H., and Hashimoto, K. (1986). Structure-toxicity relationship of monoketones. *Toxicol. Lett*. **30**,13-17.

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.

Tunç, I, Erler, F., Dagli, F., and Çalis, Ö. (1997). Insecticidal activity of acetone vapours. *J. Stored Prod. Res.* **33**,181-185.

USEPA (1994). US Environmental Protection Agency, Toxic Release Inventory Data for 1992. National Toxicology Information Program, National Library of Medicine. Bethesda, MD.

Van Duuren, B.L., Loewngart, G., Seidman, I., Smith, A.C., and Melchione, S. (1978). Mouse skin carcinogenicity tests of the flame retardants tris (2,3-dibromopropyl)phosphate, tetrakis-(hydroxymethyl)-phosphonium chloride, and polyvinyl bromide. *Cancer Res*. **38**,3236-3240.

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.

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.

Ward, J.M., Quander, R., Devor, D., Wenk, M.L., and Spangler, E.F. (1986). Pathology of aging female SENCAR mice used as controls in skin two-stage carcinogenesis studies. *Environ. Health Perspec*. **68**,81-89.

Wieland, O. (1968). Ketogenesis and its regulation. *Adv. Metab. Disorders* **3**,1-47.

Wigaeus, E., Holm, S., and Astrand, I. (1981). Exposure to acetone. Uptake and elimination in man. *Scand. J. Work Environ. Health* **7**,84-94.

Williamson, D.H. and Whitelaw, E. (1978). Physiological aspects of the regulation of ketogenesis. *Biochem. Soc. Symp.* **43**,137-161.

Winder, C. and Turner, P.J. (1993). Solvent exposure and related work practices amongst apprentice spray painters in automotive body repair workshops. *Ann. Occup. Hyg.* **36**,385-394.

Winek, C.L. (1976). Tabulation of therapeutic, toxic, and lethal concentrations of drugs and chemicals in blood. *Clin. Chem*. **22**,832-836.

Wysocki, C.J., Dalton, P., Brody, M., and Lawley, H.J. (1997). Odor and irritation thresholds for acetone in acetone-exposed factory workers and control (occupationally-nonexposed) subjects. *Am. Ind. Hyg. Assoc. J*. **58**,704-712.

Yocom, J.E., Hein, G.M., and Nelson, H.W. (1956). A study of the effluents from backyard incinerators. *J. Air Pollut. Control Assoc*. **6**,84-89.

Zakova, N., Zak, F., Froelich, 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.

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.

Zweidinger, R.B., Sigsby, J.E., Tajada, S.B., Stump, F.D., Dropkin, D.L., Ray, W.D., and Duncan, J.W. (1988). Detailed hydrocarbon and aldehyde mobile source emissions from roadway studies. *Environ. Sci. Technol*. **22**,956-962.