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HEALTH AND ENVIRONMENTAL EFFECTS DOCUMENT
FOR ACETOPHENONE

Prepared for

OFFICE OF SOLID WASTE AND
EMERGENCY RESPONSE

Prepared by

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PREFACE

Health and Environmental Effects Documents (HEEDs) are prepared for the Office of Solid Waste and Emergency Response (OSWER). This document series is intended to support listings under the Resource Conservation and Recovery Act (RCRA) as well as to provide health-related limits and goals for emergency and remedial actions under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency Program Office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched for in this document and the dates searched are included in "Appendix: Literature Searched." Literature search material is current up to 8 months previous to the final draft date listed on the front cover. Final draft document dates (front cover) reflect the date the document is sent to the Program Officer (OSWER).

Several quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Reference doses (RfDs) for chronic and subchronic exposures for both the inhalation and oral exposures. The subchronic or partial lifetime RfD, is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs during a limited time interval, for example, one that does not constitute a significant portion of the lifespan. This type of exposure estimate has not been extensively used, or rigorously defined as previous risk assessment efforts have focused primarily on lifetime exposure scenarios. Animal data used for subchronic estimates generally reflect exposure durations of 30-90 days. The general methodology for estimating subchronic RfDs is the same as traditionally employed for chronic estimates, except that subchronic data are utilized when available.

In the case of suspected carcinogens, RfDs are not estimated. A carcinogenic potency factor, or q_1^* (U.S. EPA, 1980), is provided instead. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under the CERCLA. These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity, and acute mammalian toxicity). Chemical-specific RQs reflect the lowest of these six primary criteria. The methodology for chronic toxicity and cancer-based RQs are defined in U.S. EPA, 1983 and 1986a, respectively.

EXECUTIVE SUMMARY

Acetophenone is a colorless liquid with a sweet, pungent odor (Hawley, 1981) that is sparingly soluble (0.55 wt % at 20°C) in water (Papa and Sherman, 1981). In 1981, 4.439 million pounds of acetophenone were produced in the United States by three manufacturers (USITC, 1982). Currently, five companies have been cited as operating six U.S. production facilities for this chemical (SRI, 1986). Acetophenone is used as a chemical intermediate for resins, pharmaceuticals, corrosion inhibitors and dyestuffs; as a solvent for gums, resin dyestuffs and high-melting aromatic chemicals; as a polymerization catalyst and photosensitizer in organic synthesis; as a flavoring agent for tobacco and in perfumery (Papa and Sherman, 1981; Windholz, 1983; Dorsky et al., 1963).

If acetophenone is released to water, microbial degradation and volatilization are expected to be the major environmental fate and transport processes. A number of biodegradation studies have shown that acetophenone is significantly biodegradable (Ludzack and Ettinger, 1963; Mills and Stack, 1954; Kharitonova and Sklovskaya, 1967; Urano and Kato, 1986; Dore et al., 1975; Sasaki, 1978). The volatilization half-life from a river 1 m deep flowing at 1 m/sec with a wind velocity of 3 m/sec was estimated to be 3.7 days. Hydrolysis, oxidation, adsorption to sediments and bioconcentration are not expected to be significant. When acetophenone is released to the ambient atmosphere, reaction with photochemically-produced hydroxyl radicals is expected to be the dominant removal mechanism; the half-life for this reaction has been estimated to be ~2 days (U.S. EPA, 1987). In the atmosphere, acetophenone will exist almost entirely in the vapor phase.

If acetophenone is released to soil, microbial degradation is likely to be the major degradation process. Based on various adsorption studies (Hassett et al., 1980; Briggs, 1981; Gerstl and Mingelgrin, 1984; Southworth and Keller, 1986), acetophenone is expected to be mobile in soil and susceptible to significant leaching. Acetophenone is also expected to evaporate from dry soil surfaces.

Acetophenone occurs naturally in various plant oils, in the buds of balsam poplar and in Concord grapes (Dorsky et al., 1963; Nicholas, 1973). It has been detected in drinking waters, surface waters, groundwaters and waste effluent waters (see Table 3-1). The presence of acetophenone in environmental waters is most likely the result of discharges from industrial sources. Based on various U.S. ambient air monitoring data of urban/suburban areas, an average daily inhalation intake of 4.6 µg has been estimated (Brodzinsky and Singh, 1982). Acetophenone is emitted to the atmosphere in automobile and diesel exhausts (Graedel, 1978; Hampton et al., 1982), in stack effluents from waste incineration (James et al., 1984) and by vaporization from perfumes (Abrams et al., 1975). Data were insufficient to estimate the daily human exposure to this compound from ingestion of foods and drinking water.

The only available data concerning toxicity of acetophenone to aquatic organisms were 96-hour LC_{50} values of 155 and 162 mg/ℓ for fathead minnows, Pimephales promelas (Brooke et al., 1984; Mattson et al., 1976).

Although quantitative data concerning absorption were not available, metabolism and toxicity data indicate that acetophenone is absorbed by both the gastrointestinal and respiratory tracts. Studies using rabbits indicate that acetophenone is metabolized to (-)l-phenylethanol, which is excreted in the urine as glucuronide and sulfate conjugates (Smith et al., 1954; Kiese

and Lenk, 1974). Other metabolites of acetophenone excreted in the urine are p-, m- and ω-hydroxyacetophenone, mandelic acid and hippuric acid (Kiese and Lenk, 1974).

The toxicity of acetophenone has not been well studied. No studies concerning the chronic toxicity or carcinogenicity of acetophenone were available. The subchronic toxicity studies indicate that acetophenone may be more toxic following inhalation exposure than oral exposure. Pinching and Doving (1974) found degeneration of olfactory bulbs in young rats exposed continuously to 8.89 mg/m³ for up to 3 months. This corresponds to an uptake from air of 8.6 mg/kg/day (see Table 9-1). Imasheva (1966) found changes in the ratio of chronaxies of antagonist muscle, a decrease in the albumin/globulin ratio, congestion of cardiac vessels and dystrophy of the liver in rats exposed to acetophenone continuously at 0.07 mg/m³ for 70 days. This corresponds to intake from air of 0.045 mg/kg/day. No effects were found at 0.007 mg/m³. In contrast, no effects were noted in rats fed acetophenone in the diet at levels up to 8450 ppm for 17 weeks (Hagan et al., 1967) or in rats treated at dietary levels that provided up to 102 mg/kg/day for 30 days (Smyth, 1946).

Reported oral LD_{50} values of acetophenone in rats range from 0.9-3.2 g/kg (see Table 6-1), while the median lethal concentration of acetophenone in air for mice in a 4-hour exposure was 1.2 mg/ℓ (Ovchagov, 1964). This corresponds to the intake from air of 127 mg/kg.

The only reproductive study available was a skin application study in which no effects on reproduction or development were noted in rats treated with acetophenone at 0.48 g/kg on gestation days 10-15 (Lagno and Bakhitizina, 1969).

Acetophenone tested negative in a reverse mutation assay (Elliger et al., 1984), but did cause DNA chain breaks after photosensitization (Rahn et al., 1974). The toxicological significance of the photosensitization study is uncertain.

A subchronic inhalation RfD of 0.0002 mg/m³ or 0.003 mg/day, and a chronic inhalation RfD of 0.00002 mg/m³ or 0.0003 mg/day were derived from a continuous exposure of 0.007 mg/m³ for 70 days in rats, using uncertainty factors of 100 and 1000. At 0.07 mg/m³, rats had congestion of cardiac vessels and liver dystrophy (Imasheva, 1966). Low confidence was placed in the RfDs because of inadequate reporting and lack of supporting data.

A subchronic oral RfD of 5 mg/kg/day or 300 mg/day and a chronic oral RfD of 0.5 mg/kg/day or 35 mg/day were derived from a dietary NOEL of 10,000 ppm (500 mg/kg/day) in rats for 17 weeks. This was the highest dose tested in the study by Hagan et al. (1967). Therefore, there was no LOAEL. Uncertainty factors of 100 for the subchronic RfD and 1000 for the chronic RfD were used. Low confidence was placed in these RfDs because the study did not define an effect level, the NOEL was ~50% of the oral LD_{50} for rats and supporting data were lacking.

An RQ of 100 based on chronic toxicity was derived from the subchronic inhalation study by Imasheva (1966).

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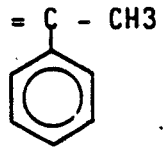
LIST OF ABBREVIATIONS

BCF	Bioconcentration factor
BOD	Biochemical oxygen demand
BODT	Biochemical oxygen demand, theoretical
CAS	Chemical Abstract Service
CS	Composite score
DNA	Deoxyribonucleic acid
K_{oc}	Soil sorption coefficient standardized with respect to organic carbon
K_{om}	Sorption coefficient standardized with respect to soil organic matter
K_{ow}	Octanol/water partition coefficient
LC_{50}	Concentration lethal to 50% of recipients
LD_{50}	Dose lethal to 50% of recipients
MED	Minimum effective dose
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect level
ppb	Parts per billion
ppm	Parts per million
ppt	Parts per thousand
RfD	Reference dose
RQ	Reportable quantity
RV_d	Dose-rating value
RV_e	Effect-rating value
UV	Ultraviolet
WS	Water solubility

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Acetophenone is the common chemical name, but this compound is also known as 1-phenylethanone, phenyl methyl ketone, acetylbenzene and hypnone (Windholz, 1983). The structure, molecular weight, empirical formula and CAS Registry number for acetophenone are as follows:



Molecular weight: 120.15

Empirical formula: C_8H_8O

CAS Registry number: 98-86-2

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Acetophenone is a colorless liquid with a sweet, pungent odor and taste (Hawley, 1981). It is freely soluble in alcohol, chloroform, ether, fatty oils and glycerol (Windholz, 1983). Selected physical properties are listed below:

Melting point:	20.5°C	Windholz, 1983
Boiling point:	201.7°C	Papa and Sherman, 1981
Specific gravity:	1.0296 (20/20°C)	Papa and Sherman, 1981
Refractive index (20°C):	1.5342	Papa and Sherman, 1981
Water solubility: at 20°C	0.55 wt % (5500 mg/ℓ)	Papa and Sherman, 1981
Vapor pressure:		
at 25°C	0.372 mm Hg	Hine and Mookerjee, 1975
at 37.1°C	1.0 mm Hg	Perry and Green, 1984
Log K_{ow}:	1.58	Hansch and Leo, 1985
Flash point:	82°C (closed cup)	Papa and Sherman, 1981
	93°C (open cup)	Papa and Sherman, 1981
Air conversion factor: (20°C)	1 mg/m³ = 0.20 ppm	Verschueren, 1983

The chemical reactions of acetophenone are typical of alkyl aryl ketones (Dorsky et al., 1963). These reactions include addition and condensation at the carbonyl group, nuclear substitution and side-chain substitution. Acetophenone is combustible (Hawley, 1981).

1.3. PRODUCTION DATA

In 1981, 4.439 million pounds of acetophenone were produced in the United States by three manufacturers (USITC, 1982); this is the most recent production figure available. In 1983, 0.733 million pounds of acetophenone were imported into the United States through principal customs districts (USITC, 1982).

Table 1-1 lists current U.S. manufacturers of acetophenone. Acetophenone can be manufactured by the oxidation of ethylbenzene or obtained as a by-product from the production of phenol using cumene oxidation (Hawley, 1981; Dorsky et al., 1963). In addition, acetophenone is produced as an intermediate by-product during the production of propylene oxide using the hydroperoxide process; however, this acetophenone is recycled and not isolated as an end-product (Kirk and Dempsey, 1982).

1.4. USE DATA

Acetophenone is used as a chemical intermediate for resins, pharmaceuticals, corrosion inhibitors and dyestuffs; as a perfume base for bath soaps; and as a solvent for gums, resin dyestuffs and high-melting aromatic chemicals (Papa and Sherman, 1981). It is also used in perfumery, in organic synthesis as a photosensitizer, as a polymerization catalyst and as a flavoring agent for tobacco (Windholz, 1983; Dorsky et al., 1963). A percentage breakdown for each individual use was not available.

TABLE 1-1

Current U.S. Manufacturers of Acetophenone*

Manufacturer	Location
Allied-Signal, Inc. (Allied Corp)	Frankford, PA
Atlantic Richfield Co.	
ARCO Specialty Chem.	West Chester, PA
Lyondell Petrochem.	Channelview, TX
Georgia Gulf Corp.	Bound Brook, NJ
Givaudian Corp.	Clifton, NJ
Texaco Inc.	El Dorado, KS

*Source: SRI, 1986

1.5. SUMMARY

Acetophenone is a colorless liquid with a sweet, pungent odor (Hawley, 1981) that is sparingly soluble (0.55 wt % at 20°C) in water (Papa and Sherman, 1981). In 1981, 4.439 million pounds of acetophenone were produced in the United States by three manufacturers (USITC, 1982). Currently, five companies have been cited as operating six U.S. production facilities for this chemical (SRI, 1986). Acetophenone is used as a chemical intermediate for resins, pharmaceuticals, corrosion inhibitors and dyestuffs; as a solvent for gums, resin dyestuffs and high-melting aromatic chemicals; as a polymerization catalyst and photosensitizer in organic synthesis; as a flavoring agent for tobacco and in perfumery (Papa and Sherman, 1981; Windholz, 1983; Dorsky et al., 1963).

2. ENVIRONMENTAL FATE AND TRANSPORT

2.1. AIR

Reaction with photochemically-produced hydroxyl radicals is expected to be the dominant removal mechanism for acetophenone in the ambient atmosphere. The half-life for this reaction is estimated to be ~2 days and is based on an average atmospheric hydroxyl radical concentration of 8×10^5 molecules/cm^3 and an estimated rate constant at 25°C of 5×10^{-12} cm^3/molecule-sec (U.S. EPA, 1987).

Based on its relatively high vapor pressure (Eisenreich et al., 1981), acetophenone is expected to exist almost entirely in the vapor phase in the atmosphere.

2.2. WATER

2.2.1. Hydrolysis. Since ketones, in general, are resistant to hydrolysis, this process is not expected to be important for acetophenone degradation in aquatic environment (Lyman et al., 1982; Lande et al., 1976).

2.2.2. Oxidation. The rate constant for the reaction of acetophenone with hydroxyl radicals in water at room temperature was ~$2.9-5.4 \times 10^9$ M^{-1}- sec^{-1} (Anbar and Neta, 1967; Dorfman and Adams, 1973). Given the assumption that natural waters have an average hydroxyl radical concentration of 10^{-17} M (Mill et al., 1980), a minimum half-life of 149 days can be estimated from the rate constant data. Therefore, the oxidation reaction will not be important in water.

2.2.3. Photolysis. Acetophenone absorbs UV light significantly in the environmentally important range of >290 nm (Draper and Crosby, 1983), which indicates a potential for direct photolysis in the environment. Irradiation of an aqueous solution of acetophenone with UV light >285 nm was shown to

produce superoxide species, while no superoxide was formed in dark controls (Draper and Crosby, 1983); however, kinetics of the potential photoalterations of aqueous acetophenone were not provided. Acetophenone can act as a photosensitizer whereby it transfers its excited state energy (obtained from UV light absorption) to a receptor molecule, and the receptor molecule undergoes alteration. The end result for the excited acetophenone is its return to the ground state without any photochemical alterations (Lande et al., 1976).

2.2.4. Microbial Degradation. Ludzack and Ettinger (1963) studied the biodegradation of acetophenone in Ohio River water. Bio-oxidation had a lag time of ~3 days and was followed by rapid carbon dioxide production. About half of the theoretical yield of carbon dioxide was recovered in 6 days following the first dose and 3 days following the second dose.

Several BOD studies found acetophenone to be significantly biodegradable. Mills and Stack (1954) measured a 10-day BODT of 56%, using a sewage seed, while Kharitonova and Sklovskaya (1967) measured a 5-day BODT of 46.1%. Urano and Kato (1986) determined a 10-day BODT of ~90% with activated sludge, using an electrolytic respirometer method and noted that ketones, in general, are changed into carboxylic acids by bio-oxidation. Dore et al. (1975) reported a 5-day BODT of 32% using three polluted surface waters as inoculum. The Japanese biodegradability tests show acetophenone to be significantly biodegradable (Sasaki, 1978).

These data indicate that biodegradation is likely to be an important, and potentially dominant, removal process for acetophenone in water.

2.2.5. Volatilization. The Henry's Law constant for acetophenone was determined to be ~0.000011 atm-m^3/mol at 25°C (Mackay et al., 1982; Hine

and Mookerjee, 1975). Using Henry's Law constant, the volatilization half-life from a river 1 m deep flowing at 1 m/sec with a wind velocity of 3 m/sec is estimated to be ~3.7 days, using the method outlined in Lyman et al. (1982). Volatilization from rivers or other bodies of water deeper than 1 m and flowing at a speed <1 m/sec will be slower.

2.2.6. **Adsorption.** Based on the adsorption to soils and sediments data (Section 2.3.3.), acetophenone is not expected to partition significantly from the water column to aquatic sediment; however, acetophenone has been detected in river bed sediment in a region of heavy industrial discharge (Steinheimer et al., 1981).

2.2.7. **Bioconcentration.** The BCF of an organic compound can be estimated from the following two recommended regression equations (Lyman et al., 1982):

$$\log BCF = 0.76 \log K_{ow} - 0.23 \qquad (2\text{-}1)$$

$$\log BCF = 2.791 - 0.564 \log WS \text{ (ppm)} \qquad (2\text{-}2)$$

Based on a $\log K_{ow}$ of 1.58 and a WS of 5500 ppm for acetophenone (see Section 1.2.), the BCF values estimated from Equations 2-1 and 2-2 are 9 and 5, respectively. These BCF values indicate that bioconcentration in aquatic organisms is not expected to be significant.

2.3. SOIL

2.3.1. **Microbial Degradation.** Experimental soil studies were not found; however, microbial degradation data (see Section 2.2.4.) suggest that significant biodegradation of acetophenone is likely to occur in soil.

2.3.2. **Chemical Degradation.** Pertinent data regarding the chemical degradation of acetophenone in soil could not be located in the reviewed literature and data bases as cited in Appendix A. Based on water-related data, hydrolysis and oxidation are not expected to be significant. Therefore, microbial degradation is likely to be the major degradation process in soil.

2.3.3. Adsorption/Leaching. The adsorption of acetophenone by soils has been studied by several investigators. Hassett et al. (1980) determined K_{oc} values of 22-95 in 14 soils and sediments collected from Ohio, Missouri, Mississippi and Illinois rivers and their watersheds with organic carbon contents ranging from 0.11-2.38%. Briggs (1981) measured a Freundlich adsorption coefficient of 0.42 for an Australian soil of 1.09% organic matter content, which corresponds to a K_{oc} value of 66. Gerstl and Mingelgrin (1984) determined an average K_{om} value of 21.9 (corresponds to a K_{oc} of 37.8) for 12 soils and sediments with organic matter content ranging from 0.11-7.85%. Southworth and Keller (1986) determined K_{oc} values of 105-270 for three soils from West Virginia and Tennessee.

K_{oc} values <150 indicate high soil mobility, while values between 150 and 500 indicate medium soil mobility (Swann et al., 1983). Therefore, acetophenone is expected to be mobile in soil and susceptible to significant leaching.

2.3.4. Volatilization. The vapor pressure of acetophenone (0.372 mm Hg at 25°C) suggests that evaporation from dry surfaces may occur; however, the relative significance of volatilization from moist soils is not clear.

2.4. SUMMARY

If acetophenone is released to water, microbial degradation and volatilization are expected to be the major environmental fate and transport processes. A number of biodegradation studies have shown that acetophenone is significantly biodegradable (Ludzack and Ettinger, 1963; Mills and Stack, 1954; Kharitonova and Sklovskaya, 1967; Urano and Kato, 1986; Dore et al., 1975; Sasaki, 1978). The volatilization half-life from a river 1 m deep flowing at 1 m/sec with a wind velocity of 3 m/sec was estimated to be

3.7 days. Hydrolysis, oxidation, adsorption to sediments and bioconcentration are not expected to be significant. If acetophenone is released to the ambient atmosphere, reaction with photochemically-produced hydroxyl radicals is expected to be the dominant removal mechanism; the half-life for this reaction has been estimated to be ~2 days (U.S. EPA, 1987). In the atmosphere, acetophenone will exist almost entirely in the vapor phase. If acetophenone is released to soil, microbial degradation is likely to be the major degradation process. Based on various adsorption studies (Hassett et al., 1980; Briggs, 1981; Gerstl and Mingelgrin, 1984; Southworth and Keller, 1986), acetophenone is expected to be mobile in soil and susceptible to significant leaching. Acetophenone is expected to evaporate from dry soil surfaces.

3. EXPOSURE

Acetophenone occurs naturally in oil of castoreum, oil of labdanum resin and oil of Stirlingia latifolia, in the buds of balsam poplar (Dorsky et al., 1963), and in Concord grape essence (Nicholas, 1973). The heavy-oil fraction of coal tar contains small amounts of acetophenone (Dorsky et al., 1963).

3.1. WATER

Table 3-1 lists various water monitoring data for acetophenone. Acetophenone has been detected in drinking water, surface and groundwaters, and waste effluent waters. The data for drinking water are insufficient to accurately estimate an average daily intake for humans. The U.S. EPA STORET Data Base contains 13 reported observations for acetophenone, with maximum and minimum concentrations of 72 and 1 ppb, respectively, and a mean concentration of 11.3 ppb (U.S. EPA, 1986b).

The presence of acetophenone in the various environmental waters reported in Table 3-1 is most likely the result of discharges from industrial sources. Abrams et al. (1975) suggested that acetophenone could also be formed in groundwaters or drinking waters by the decomposition of phenyl methyl carbinol.

3.2. FOOD

Limited food monitoring data regarding acetophenone were located. Acetophenone was 1 of 187 organic compounds detected in roasted filbert nut volatiles (Kinlin et al., 1972). Pellizzari et al. (1982) detected acetophenone in 8/8 mother's milk samples collected from volunteers in Bridgeville, PA, Bayonne and Jersey City, NJ, and Baton Rouge, LA.

TABLE 3-1

Water Monitoring Data for Acetophenone

Type of Water	Location	Concentration	Sampling Dates/Remarks	Reference
Drinking	Philadelphia, PA	1.0 ppb	August 1974	Keith et al., 1976
	Philadelphia, PA	NR	April 1975	Suffet et al., 1976
	Philadelphia, PA	NR	August, November 1976; January 1977	Suffet et al., 1980
Drinking[a]	Poplarville, MS	NR	March 1979	Lucas, 1984
	Cincinnati, OH	NR	October 1978, January 1980	
	Miami, FL	NR	February 1977	
	New Orleans, LA	NR	January 1976	
	Philadelphia, PA	NR	February 1976	
	Ottumwa, IO	NR	September 1976	
	Seattle, WA	NR	November 1976	
Drinking	Japan	5.4 ppb	NR	Shinohara et al., 1981
River	204 sites in United States	1-2 ppb[b]	August 1975-September 1976; compound detected in 6/204 sites; all sites were from 14 heavily industrialized river basins	Ewing et al., 1977
River	Kanawha River, Nitro, WV	NR	1959	Rosen et al., 1963
River	England	NR	June 1978	Fielding et al., 1981
River	Waal River, Netherlands	NR	October 1974	Meijers and Vanderleer, 1976
River	Japan	NR	NR	Akiyama et al., 1980
Sea	Japan	NR	NR	Akiyama et al., 1980
Lake	Lake Michigan	1-2 ppb	NR	Konasewich et al., 1978
River bed sediment	Calcasieu River (near Lake Charles, LA)	NR	November 1979; in area of heavy industrial discharge	Steinheimer et al., 1981
Ground	Australia	NR	1975; an aquifer near quarry holes used to dump organic wastes	Stepan et al., 1981
Ground	Netherlands	<0.1-10 ppb	1976-1978; percolate of a waste tip area	Zoeteman et al., 1981

TABLE 3-1 (cont.)

Type of Water	Location	Concentration	Sampling Dates/Remarks	Reference
Effluent	Rosell and Sauget, IL	NR	May, June 1980; secondary effluents from municipal treatment plants	Ellis et al., 1982
Effluent	Louisiana	NR	1970; wastewater discharge from a petrochemical plant	Keith, 1974
Effluent	Louisiana	NR	1970; textile plant effluent	Shackelford and Keith, 1976
	Louisville, KY	NR	March 1974; latex and chemical plant effluents	
	Memphis, TN	NR	August 1974; chemical plant effluent	
	Newport, TN	NR	June 1973; chemical plant effluent	
Effluent	Queensland, Australia	10 ppm	wastewater from shale oil processing	Dobson et al., 1985
Effluent	Soviet Union	NR	wastewater from propylene oxide manufacture	Mamedova et al., 1973

[a]Concentration range where the compound was detected

[b]Tentative identification from concentrated samples

NR = Not reported

3.3. INHALATION

Brodzinsky and Singh (1982) compiled various U.S. ambient air monitoring data pertaining to acetophenone. Seven air samples from rural/remote areas contained no acetophenone, three samples from urban/suburban areas contained a mean concentration of 46 ppt and 66 samples from source dominated areas contained a mean concentration 750 ppt. Smeyers-Verbeke et al. (1984) detected acetophenone in the ambient air of Delft, Netherlands.

Assuming an average acetophenone concentration of 46 ppt (0.230 $\mu g/m^3$) in a typical urban/suburban atmosphere, an average daily intake of 4.6 μg can be calculated assuming a daily intake of 20 m^3 of air.

Acetophenone is released to the atmosphere in automobile and diesel exhausts, and in plant volatiles (Hampton et al., 1982; Graedel, 1978). In addition, it has been detected as a combustion product of waste incineration (James et al., 1984) and may therefore be present in incineration stack effluents. Abrams et al. (1975) cited vaporization from perfumes as an emission source.

3.4. DERMAL

Pertinent data regarding the monitoring of dermal exposure to acetophenone could not be located in the available literature as cited in Appendix A.

3.5. SUMMARY

Acetophenone occurs naturally in various plant oils, in the buds of balsam poplar and in Concord grapes (Dorsky et al., 1963; Nicholas, 1973). It has been detected in drinking waters, surface waters, groundwaters and waste effluent waters (see Table 3-1). The presence of acetophenone in environmental waters is most likely the result of discharges from industrial

sources. Based on various U.S. ambient air monitoring data of urban/ suburban areas (Brodzinsky and Singh, 1982), an average daily inhalation intake of 4.6 μg has been estimated. Acetophenone is emitted to the atmosphere in automobile and diesel exhausts (Graedel, 1978; Hampton et al., 1982), in stack effluents from waste incineration (James et al., 1984) and by vaporization from perfumes (Abrams et al., 1975). Data were insufficient to estimate the daily human exposure to this compound from ingestion of foods and drinking water.

4. AQUATIC TOXICITY

4.1. ACUTE TOXICITY

The only available data concerning the toxicity of acetophenone to aquatic organisms were 96-hour LC_{50} values of 155 and 162 mg/ℓ for fathead minnows, Pimephales promelas (Brooke et al., 1984; Mattson et al., 1976).

4.2. CHRONIC EFFECTS

Pertinent data regarding the toxicity of acetophenone to aquatic organisms could not be located in the available literature as cited in Appendix A.

4.3. PLANT EFFECTS

Pertinent data regarding the toxicity of acetophenone to aquatic plants could not be located in the available literature as cited in Appendix A.

4.4. SUMMARY

The only available data concerning the toxicity of acetophenone to aquatic organisms were 96-hour LC_{50} values of 155 and 162 mg/ℓ for fathead minnows, Pimephales promelas (Brooke et al., 1984; Mattson et al., 1976).

5. PHARMACOKINETICS

5.1. ABSORPTION

Quantitative data regarding the absorption of acetophenone could not be located in the available literature as cited in Appendix A. An oral study (Sections 5.3. and 5.4.) and an inhalation study (Section 6.1.1.) resulting in systemic toxicity indicate that acetophenone is absorbed by the gastrointestinal and respiratory tracts.

5.2. DISTRIBUTION

Pertinent data regarding the distribution of acetophenone could not be located in the available literature as cited in Appendix A.

5.3. METABOLISM

Smith et al. (1954) examined the urinary metabolites of acetophenone in chinchilla rabbits treated by gavage with acetophenone in water, and found that acetophenone was metabolized to (-)l-phenylethanol glucuronide and the sulfate.

Kiese and Lenk (1974) also examined the metabolism of acetophenone in rabbits. Male rabbits were injected intraperitoneally with a total of 5.36 g of acetophenone, and the urine was collected for 48 hours and examined for metabolites both before and after incubation with glucuronidase. The urinary metabolites identified were (-)l-phenylethanol and ω-hydroxyacetophenone. About half of the l-phenylethanol was excreted unconjugated, while the remaining was identified following incubation with glucuronidase. p-Hydroxyacetophenone, m-hydroxyacetophenone and phenols were also identified in the urine. Using these data and the data of Thierfelder and Daiber (1923) and Thierfelder and Klenk (1924), who found hippuric acid and mandelic acid in the urine of rabbits treated with acetophenone, Kiese and Lenk (1974) proposed the pathway presented in Figure 5-1.

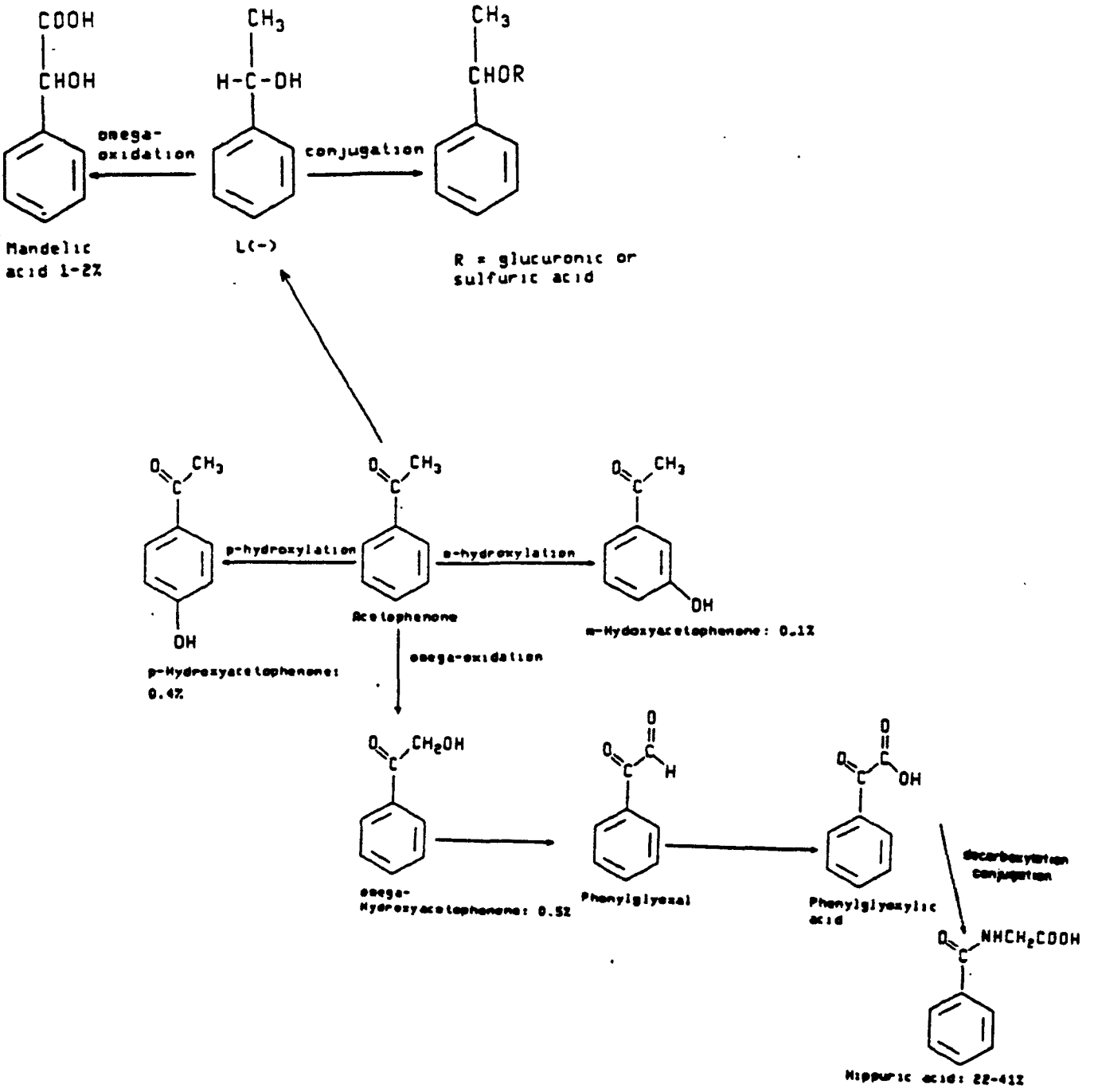


FIGURE 5-1

Proposed Metabolic Pathway in the Rabbit

Source: Kiese and Lenk, 1974

Leibman (1971) studied the metabolism of acetophenone in preparations of rat and rabbit liver cytosol and microsomes. He found that in the presence of NADPH, acetophenone was reduced to 1-phenylethanol. When NADPH was removed from the system, the amount of 1-phenylethanol was greatly decreased. Studies using preparations from rabbit livers revealed that most of the reducing activity was in the cytosol fraction rather than the microsomes. Acetophenone reducing activity, although not as great as in the liver, was also found in cytosol preparations of rabbit kidney, heart and lung, but not in the brain. Leibman (1971) also found that pretreatment of rats with phenobarbital did not affect the rate of acetophenone reduction by homogenates of the liver.

The enzymes involved in the reduction of acetophenone are alcohol dehydrogenase and aromatic aldehyde-ketone reductase (Lande et al., 1976). An additional enzyme, α,β-unsaturated ketone reductase, which is involved in the reduction of other ketones, was shown to be inactive in the reduction of acetophenone in vitro in a study using enzyme isolated from dog erythrocytes and human liver (Fraser et al., 1967).

5.4. EXCRETION

Smith et al. (1954) found that ~47% of an oral dose of acetophenone (450 mg/kg) administered to rabbits was excreted in the urine as (-)1-phenylethanol glucuronide, while 3% was excreted as the sulfate. The excretion of the glucuronide was nearly complete 1 day after dosing.

Analysis of rabbit urine 48 hours after an intraperitoneal injection of acetophenone revealed that ~3.6% of the dose was excreted as 1-phenylethanol (both free and conjugated), and ~0.95% was excreted as ω-hydroxyacetophenone (Keise and Lenk, 1974). About 0.012% of the dose was recovered from

the urine as unmetabolized acetophenone. Other urinary metabolites which comprised <1% of the administered dose were p-hydroxyacetophenone, m-hydroxyacetophenone and phenols, and ~22-41% is hippuric acid.

5.5. SUMMARY

Although quantitative data concerning absorption were not available, metabolism and toxicity data indicate that acetophenone is absorbed by both the gastrointestinal and respiratory tracts. Studies in rabbits indicate that acetophenone is metabolized to (-)l-phenylethanol, which is excreted in the urine as glucuronide and sulfate conjugates (Smith et al., 1954; Kiese and Lenk, 1974). Other metabolites of acetophenone excreted in the urine are p-, m- and ω-hydroxyacetophenone, mandelic acid and hippuric acid (Kiese and Lenk, 1974).

6. EFFECTS

6.1. SYSTEMIC TOXICITY

6.1.1. Inhalation Exposures.

6.1.1.1. **SUBCHRONIC** -- Pinching and Doving (1974) exposed groups of four Wistar rats (2 weeks of age at start of experiment) to acetophenone vapor at 7.4×10^{-8} M (8.89 mg/m³) continuously for periods varying from 1 week to 3 months. Similar groups of rats, exposed to filtered air, were maintained as controls. The rats were sacrificed at ~1, 2 or 3 months of age and examined for degeneration of olfactory bulb cells. The results showed that acetophenone exposure caused a specific pattern of degeneration of olfactory bulb cells. The degeneration noted was principally a darkening and shrinkage of cell bodies and did not involve cell death. The patterns of degeneration did not change with increasing exposure period, but changes were better defined and more marked after 2 months than at earlier periods. No other parameters were examined.

In a Russian study (Imasheva, 1966), groups of 15 white male rats were exposed continuously to acetophenone vapor at 0, 0.007 or 0.07 mg/m³ for 70 days. The behavior, body weights and chronaxy of antagonist muscles of all rats were examined. In addition, cholinesterase activity and protein fractions of the blood serum of five rats/group were examined. After the exposure period, some of the rats (number unspecified) from each group were sacrificed and histological examinations of unspecified organs were made. The results of the study revealed no changes in the parameters examined in rats exposed to 0.007 mg/m³. Rats exposed to 0.07 mg/m³ showed changes in the ratio of chronaxies of antagonist muscles and a decrease in the albumin/globulin ratio of the blood, with no change in the amount of total protein. Changes in cholinesterase activity were also observed in the high-

dose group but were inconsistent; several rats showed a depression of activity, while an increase in activity was observed in one rat. Histopathological examination of the high-dose rats revealed congestion of the cardiac vessels and pronounced dystrophy of the liver.

6.1.1.2. CHRONIC -- Pertinent data regarding the chronic inhalation toxicity of acetophenone could not be located in the available literature as cited in Appendix A.

6.1.2. Oral Exposures.

6.1.2.1. ACUTE -- Reported oral LD_{50} values of acetophenone in rats range from 0.9-3.2 g/kg (Table 6-1), while the median lethal concentration of acetophenone in air for mice in a 4-hour exposure was 1.2 mg/ℓ (Ovchagov, 1964).

6.1.2.2. SUBCHRONIC -- In a 30-day study, Smyth (1946) fed groups of five male and five female albino rats acetophenone in the diet at levels of 0, 0.003, 0.0125, 0.05 or 0.2%. As determined by the author, these dietary levels provided the rats with doses of 0, 1, 6, 25 or 102 mg/kg/day. The acetophenone was added to the diet in lard. No dose-related changes were noted in the amount of food eaten, growth, fatness, liver or kidney weights, blood urea or micropathology of unspecified organs.

Hagan et al. (1967) fed groups of 10 male and 10 female weanling Osborne-Mendel rats commercially-available acetophenone in the diet at 0, 1000, 2500 or 10,000 ppm (0, 50, 125, 500 mg/kg bw) for 17 weeks. During a 7-day period, ~31% of the acetophenone was lost from the diet by volatilization, so that the mean loss was ~15.5%. Adjusting for the loss of acetophenone, the mean weekly levels of acetophenone in the food were 0, 845, 2113 or 8450 ppm. The results of the study revealed no treatment-related effects. The parameters examined were body weight, organ weights, hematology and macroscopic examinations at sacrifice.

TABLE 6-1

Acute Oral Toxicity of Acetophenone

Species	Dose (g/kg)	Dilution/Vehicle	Mortality Data	Reference
Rat	3.0	NS	14-day LD_{50}	Smyth and Carpenter, 1944
Rat	0.9	20% in 1% Tergitol®†	14-day LD_{50}	Smyth, 1946
Rat	2.2	undiluted	14-day LD_{50}	Mellon Institute, 1956
Rat	1.07	propylene glycol	14-day LD_{50}	Mellon Institute, 1956
Rat	3.2	undiluted	14-day LD_{50}	Jenner et al., 1964
Rat	2.55	undiluted	14-day LD_{50}	Smyth et al., 1969
Rat	1.03	NS	LD_{50}	E.I. Dupont DeNemours and Co., 1983
Rabbit	1.76	NS	14-day LD_{50}	Mellon Institute, 1956

†An aqueous solution of 25% sodium 3,9-diethyl-6-trideconal sulfate used as a dispersing agent.

NS = Not specified

Comprehensive microscopic examinations of 6-8 males and 6-8 females of the high-dose and control groups also revealed no changes.

6.1.2.3. CHRONIC -- Pertinent data regarding the chronic oral toxicity of acetophenone could not be located in the available literature as cited in Appendix A.

6.1.3. Other Relevant Information. Smyth et al. (1969) studied the joint toxic action of equal volumes of a number of chemicals by gavage in female albino rats. When acetophenone was mixed with an equal volume of tetrachloroethylene or acetonitrile the effect was more than additive, as determined by the ratios of the predicted to the observed LD_{50}.

Abstracts of Russian studies describe investigations of the toxicity of acetophenone vapor in combination with benzene (Tsulaya, 1967), phenol (Korneev, 1967) or acetone (Tkach, 1967). Rats exposed to benzene vapor at 0.9 mg/m³ and acetophenone at 0.003 mg/m³ for 84 days showed no changes in muscular chronaxy, concentrations of nucleic acids in the blood, 17-ketosteroids in the urine or changes in leukocyte and erythrocyte counts (Tsulaya, 1967). Korneev (1967) stated that a mixture of 0.00747 mg/m³ phenol and 0.00517 mg/m³ acetophenone affected visual acuity in humans, while 0.00759 mg/m³ phenol and 0.00357 mg/m³ acetophenone had an effect on cerebral potential. Animals (species unspecified) exposed to phenol at 0.0637 mg/m³ and acetophenone at 0.01732 mg/m³ showed changes in cholinesterase activity, motor muscle-antagonist chronaxy, pronounced eosinopenia, porphyrin metabolism and urine 17-ketosteroid content. Chronic continuous exposure of rats to acetophenone and acetone at fractions of their olfactory thresholds (thresholds = 1.096 mg/m³ acetone, 0.01 mg/m³ acetophenone) resulted in "subordination of brain function to motor chronaxy of the muscle antagonists, depressed blood cholinesterase activity, increased urinary

coproporphyrin and 17-ketosteroids and reduction of blood eosinophils" (Tkach, 1967).

Imasheva (1966) exposed three human subjects to acetophenone to determine the effect of exposure on light sensitivity of the eye. At 0.02 mg/m³, acetophenone caused a decrease in light sensitivity in all three subjects, while acetophenone at 0.007 mg/m³ was inactive.

Rats exposed to a mist of acetophenone at 21-24 mg/ℓ (21,000-24,000 mg/m³) for 2 hours survived, but 6/6 rats died after 4 hours of exposure. The deaths of these rats were attributed to anesthesia; the lungs, kidneys and liver of these animals were congested (Smyth, 1946).

E.I. Dupont DeNemours and Co. (1983) and Smyth (1946) reported that six rats exposed to acetophenone at 210 ppm (1032 mg/m³) for 8 hours survived the exposure. Ovchagov (1964) stated that the median lethal concentration of acetophenone for mice in a 4-hour exposure was 1.2 mg/ℓ.

The acute oral toxicity of acetophenone has been studied by a number of investigators. The toxicity values found are presented in Table 6-1.

6.2. CARCINOGENICITY

Pertinent data regarding the carcinogenicity of acetophenone could not be located in the available literature as cited in Appendix A.

6.3. MUTAGENICITY

Acetophenone tested negative for reverse mutations in Salmonella typhimurium strains TA100, TA98 and TA1537 both with and without rat S-9 metabolic activation in a plate incorporation assay at levels up to 3000 nmol/plate (Elliger et al., 1984).

Rahn et al. (1974) found that acetophenone caused DNA chain breaks in DNA isolated from Escherichia coli strain B(3)T⁻ after photosensitization.

6.4. TERATOGENICITY

In a study by Lagno and Bakhtizina (1969), summarized by Krasavage et al. (1982), acetophenone applied to the skin of pregnant rats at 0.48 mg/kg on gestation days 10-15 did not result in any changes in the gestation period, size of litters, weight of offspring, or time of appearance of hair or teeth, opening of eyes, or the appearance of reflexes.

6.5. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding other reproductive effects of acetophenone could not be located in the available literature as cited in Appendix A.

6.6. SUMMARY

The toxicity of acetophenone has not been well studied. No studies concerning the chronic toxicity or carcinogenicity of acetophenone were available. The subchronic toxicity studies indicate that acetophenone may be more toxic following inhalation exposure than oral exposure. Pinching and Doving (1974) found degeneration of olfactory bulbs in young rats exposed continuously to 8.89 mg/m^3 for up to 3 months. Imasheva (1966) found changes in the ratio of chronaxies of antagonist muscle, a decrease in the albumin/globulin ratio, congestion of cardiac vessels and dystrophy of the liver in rats exposed to acetophenone continuously at 0.07 mg/m^3 for 70 days. No effects were found at 0.007 mg/m^3. In contrast, no effects were noted in rats fed acetophenone in the diet at levels up to 8450 ppm for 17 weeks (Hagan et al., 1967), or in rats treated at dietary levels that provided up to 102 mg/kg/day for 30 days (Smyth, 1946).

The only reproductive study available was a skin application study in which no effects on reproduction or development were noted in rats treated with acetophenone at 0.48 g/kg on gestation days 10-15 (Lagno and Bakhitizina, 1969).

Acetophenone tested negative in a reverse mutation assay (Elliger et al., 1984), but did cause DNA chain breaks after photosensitization (Rahn et al., 1974). The toxicological significance of the photosensitization study is uncertain.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

Acetophenone is regarded as a safe food additive (U.S. FDA, 1975). Other guidelines and standards, including EPA ambient water and air quality criteria, drinking water standards, FAO/WHO ADIs, EPA or FDA tolerances for raw agricultural commodities or food, and ACGIH, NIOSH or OSHA occupational exposure limits could not be located in the available literature as cited in Appendix A.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the effects of acetophenone could not be located in the available literature as cited in Appendix A.

8. RISK ASSESSMENT

8.1. CARCINOGENICITY

8.1.1. All Routes. Pertinent data regarding the carcinogenicity of acetophenone following inhalation, oral or other routes of exposure could not be located in the available literature as cited in Appendix A.

8.1.2. Weight of Evidence. Acetophenone has not been examined in any carcinogenicity studies; therefore, acetophenone can be placed in EPA Group D, no data for carcinogenicity available (U.S. EPA, 1986c).

8.1.3. Quantitative Risk Assessment. Pertinent data regarding the carcinogenicity of acetophenone could not be located in the available literature; therefore, quantitative risk assessment based on carcinogenicity cannot be conducted.

8.2. SYSTEMIC TOXICITY

8.2.1. Inhalation Exposure.

8.2.1.1. LESS-THAN-LIFETIME EXPOSURES (SUBCHRONIC) -- Pinching and Doving (1974) examined the effect of acetophenone exposure on the olfactory bulb. A specific pattern of degeneration of cells of the olfactory bulb was noted in rats exposed to acetophenone at 8.89 mg/m³ for up to 3 months. Because this study did not define a NOAEL and because olfactory bulb degeneration was the only parameter examined, this study is inadequate for risk assessment.

The only other inhalation study of acetophenone available was reported by Imasheva (1966). In this study, groups of 15 male rats were exposed to acetophenone continuously at 0, 0.007 or 0.07 mg/m³ for 70 days. No effects were observed in rats exposed to 0.007 mg/m³. At 0.07 mg/m³, congestion of cardiac vessels and liver dystrophy were noted. Rats also showed changes in the ratio of chronaxies of antagonist muscles and a

decrease in the albumin/globulin ratio of the blood, with no change in the amount of total protein. The corresponding NOAEL in rats is 0.0045 mg/kg/day. Using an uncertainty factor of 100 (10 for interspecies extrapolation and 10 for intraspecies variability), a tentative subchronic inhalation RfD of 0.00004 mg/kg/day can be obtained. For a 70 kg human that corresponds to 0.003 mg/day. This corresponds to an air concentration of 0.0002 mg/m^3.

The level of confidence in the subchronic inhalation RfD is low because there are no studies that support the findings of the Imasheva (1966) study. In addition, the Imasheva (1966) study used only male rats, and although 15 rats were used per dose group, only 5/group were used to study cholinesterase activity and serum protein levels, while histopathological examinations were conducted on an unspecified number of rats.

8.2.1.2. CHRONIC EXPOSURES -- Pertinent data regarding the chronic exposure of acetophenone could not be located in the available literature as cited in Appendix A. A chronic inhalation RfD can be estimated from the subchronic inhalation study using an additional uncertainty factor of 10. Applying the additional uncertainty factor, the chronic inhalation RfD for acetophenone is 0.000005 mg/kg/day or 0.0003 mg/day, corresponding to an air concentration of 0.00002 mg/m^3.

8.2.2. Oral Exposure.

8.2.2.1. LESS-THAN-LIFETIME EXPOSURES (SUBCHRONIC) -- In the 30-day study by Smyth (1946), no effects were noted in rats fed acetophenone in the diet at levels of 0, 1, 6, 25 or 102 mg/kg/day. The only other subchronic study available was the 17-week study by Hagan et al. (1967) in which no effects were noted in rats fed diets containing acetophenone at 0, 50, 125 or 500 mg/kg/day. Neither study defines an effect level, but because the Hagan et al. (1967) study was longer and because higher dose levels were used, it is more appropriate for the derivation of the RfD.

Assuming a rat consumes a daily amount of food equivalent to 5% of its body weight (U.S. EPA, 1986d), the high-dose rats consumed acetophenone at ~500 mg/kg/day. Applying an uncertainty factor of 100 (10 for species-to-species extrapolation and 10 to protect sensitive humans), a subchronic RfD of 5 mg/kg/day or 350 mg/day for a 70 kg human is derived.

The level of confidence in the subchronic RfD is low. The Hagan et al. (1967) study used only 10 male and 10 female rats/dose group, and only 6-8 rats of each sex of just the high-dose group were examined microscopically. The Hagan et al. (1967) study did not define an effect level, and the NOEL was near the oral LD_{50} for rats, which ranges from 0.9-3.2 g/kg. In addition, other data to support this RfD were not located in the available literature. Since acetophenone has not been tested for carcinogenicity, teratogenicity or other reproductive effects, it is uncertain whether the RfD will be protective.

8.2.2.2. CHRONIC EXPOSURES -- Pertinent data regarding the oral chronic exposure of acetophenone could not be located in the available literature as cited in Appendix A. However, a chronic RfD can be derived by dividing the subchronic RfD by an additional uncertainty factor of 10 to extrapolate from subchronic to chronic exposure. Dividing the subchronic RfD derived from the Hagan et al. (1967) study by 10, a chronic RfD of 0.5 mg/kg/day or 35 mg/day for a 70 kg human is derived. The level of confidence in this RfD is low for reasons stated previously (see Section 8.2.2.1.) and because the study was subchronic.

9. REPORTABLE QUANTITIES

9.1. BASED ON SYSTEMIC TOXICITY

The toxicity of acetophenone was discussed in Chapter 6. The only toxicity studies in which toxic effects were observed were the inhalation studies, which are summarized in Table 9-1.

Pinching and Doving (1974) observed olfactory bulb degeneration in rats exposed continuously to 8.89 mg/m³ for up to 3 months. Since this was the only exposure level investigated, it is not known if olfactory bulb degeneration would occur at a lower exposure level; therefore, the MED for this effect is not known. Furthermore, olfactory bulb degeneration was the only endpoint examined. Since Imasheva (1966) observed liver dystrophy and cardiac vessel congestion at a continuous exposure level of 0.07 mg/m³, it is possible that the rats in the Pinching and Doving (1974) study also had systemic effects. Imasheva (1966) did not observe effects at 0.007 mg/m³. Thus, an RQ can be derived from the Imasheva (1966) study. The effects at 0.07 mg/m³ warrant an RV_e of 5. The exposure level is equivalent to a human dose of 0.008 mg/kg/day (see Table 9-1), which when multiplied by 70 kg and divided by an uncertainty factor of 10 to approximate chronic exposure equals the MED of 0.056 mg/day (Table 9-2). The MED corresponds to an RV_d of 7.4. Multiplying the RV_d by the RV_e yields the CS of 37, which corresponds to an RQ of 100 (Tables 9-2 and 9-3).

9.2. BASED ON CARCINOGENICITY

Pertinent data regarding the carcinogenicity of acetophenone were not available; therefore, an RQ based on carcinogenicity is not warranted.

TABLE 9-1

Toxicity Summary for Acetophenone

Species/ Strain	Sex	No. at Start	Average Weight (kg)	Vehicle/ Physical State	Purity	Exposure	Transformed Animal Dose (mg/kg/day)	Transformed Human Dose[a] (mg/kg/day)	Response	Reference
Rat/white	M	15	0.35[b]	air	NR	0.07 mg/m³ continuously for 70 days	0.045[c]	0.008	Dystrophy of liver, congestion of cardiac vessels, changes in ratio of chronaxies of muscle antagonists	Imasheva, 1966
Rat/Wistar	NR	4/group	0.10[d]	air	NR	8.89 mg/m³	8.6[e]	0.97	Degeneration of olfactory bulb	Pinching and Doving, 1974

[a]Calculated by multiplying the animal transformed dose by the cube root of the ratio of the animal body weight to the human body weight (70 kg).

[b]Reference rat weight (U.S. EPA, 1986c)

[c]Calculated assuming a 0.35 kg rat breathes 0.223 m³ of air/day.

[d]The rats were 2 weeks old at the beginning of the study and weighed ~0.03 kg. Assuming that a young rat grows rapidly, an average body weight of 0.1 kg was estimated.

[e]Calculated using an inhalation rate of 0.097 m³/day, which was calculated according to U.S. EPA (1980).

NR - Not reported

TABLE 9-2

Inhalation Composite Scores for Acetophenone Using Rat Toxicity Data[a]

Animal Dose (mg/kg/day)	Chronic Human MED[b] (mg/day)	RV_d	Effects	RV_e	CS	RQ
0.045	0.056	7.4	Dystrophy of the liver, decrease in albumin/globulin ratio, congestion of cardiac vessels	5	37	100

[a]Source: Imasheva, 1966

[b]The dose was divided by an uncertainty factor of 10 to approximate chronic exposure.

TABLE 9-3

Acetophenone

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:	inhalation
Dose*:	0.056 mg/day
Effect:	dystrophy of the liver, decrease in albumin/globulin ratio
Reference:	Imasheva, 1966
RV_d:	7.4
RV_e:	5
Composite Score:	37
RQ:	100

*Equivalent human dose

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APPENDIX A

LITERATURE SEARCHED

This HEED is based on data identified by computerized literature searches of the following:

TSCATS
CASR online (U.S. EPA Chemical Activities Status Report)
TOXLINE
TOXBACK 76
TOXBACK 65
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP
NTIS
Federal Register

These searches were conducted in December, 1986. In addition, hand searches were made of Chemical Abstracts (Collective Indices 5-9), and the following secondary sources should be reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1986. Documentation of the Threshold Limit Values and Biological Exposure Indices, 5th ed. Cincinnati, OH.

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Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

Windholz, M., Ed. 1983. The Merck Index, 10th ed. Merck and Co., Inc., Rahway, NJ.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

Battelle's Columbus Laboratories. 1971. Water Quality Criteria Data Book. Volume 3. Effects of Chemicals on Aquatic Life. Selected Data from the Literature through 1968. Prepared for the U.S. EPA under Contract No. 68-01-0007. Washington, DC.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Summaries of Toxicity Tests Conducted at Columbia National Fisheries Research Laboratory. 1965-1978. U.S. Dept. Interior, Fish and Wildlife Serv. Res. Publ. 137, Washington, DC.

McKee, J.E. and H.W. Wolf. 1963. Water Quality Criteria, 2nd ed. Prepared for the Resources Agency of California, State Water Quality Control Board. Publ. No. 3-A.

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APPENDIX B

Summary Table for Acetophenone

	Species	Exposure	Effect	RfD or q_1*	Reference
Inhalation Exposure					
Subchronic	rat	0.007 mg/m³ continuously for 70 days (0.004 mg/kg/day)	congestion of cardiac vessels, dystrophy of liver, decrease in albumin/globulin ratio at 0.07 mg/m³	0.0002 mg/m³ or 0.003 mg/day	Imasheva, 1966
Chronic	rat	0.007 mg/m³ continuously for 70 days (0.004 mg/kg/day)	congestion of cardiac vessels, dystrophy of liver, decrease in albumin/globulin ratio at 0.07 mg/m³	0.00002 mg/m³ or 0.0003 mg/day	Imasheva, 1966
Carcinogenicity				ID	
Oral Exposure					
Subchronic	rat	10,000 ppm in diet for 17 weeks	free-standing NOEL	5 mg/kg/day or 350 mg/day for 70 kg human	Hagan et al., 1967
Chronic	rat	10,000 ppm in diet for 17 weeks	free-standing NOEL	0.5 mg/kg/day or 35 mg/day for 70 kg human	Hagan et al., 1967
Carcinogenicity				ID	
REPORTABLE QUANTITIES					
Based on Chronic Toxicity:		100 pounds			Imasheva, 1966
Based on Carcinogenicity:		ID			

ID = Insufficient Data