UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES, AND TOXIC SUBSTANCES

July 6, 2006

ACTION MEMORANDUM

SUBJECT: Reassessment of the One Exemption from the Requirement of a Tolerance for Acetophenone (CAS Reg. No. 98-86-2)

FROM: Pauline Wagner, Chief
Inert Ingredient Assessment Branch
Registration Division (7505P)

TO: Lois A. Rossi, Director
Registration Division (7505P)

I. FQPA REASSESSMENT ACTION

Action: Reassessment of one inert exemption from the requirement of a tolerance. The reassessment decision is to maintain the inert tolerance exemption "as-is."

Chemical: Acetophenone

CFR: 40 CFR part 180.920

CAS Registry Number and Name: 98-86-2; Acetophenone

Use Summary: The major use of acetophenone is as a catalyst for the polymerization of olefins; in organic synthesis, especially as a photosensitizer and as a specialty solvent for plastics and resins. It is also a chemical intermediate for the odorant ethyl methyl phenylglycidate, the riot control agent 2-chloroacetophenone, 2-bromoacetophenone for dyes, and 3-nitroacetophenone. It is used in the manufacture of pharmaceuticals, rubber, dyestuffs, and corrosion inhibitors.

List Reclassification Determination: The current List Classification for acetophenone is 4B and it remains unchanged.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the one exemption from the requirement of a tolerance for the inert ingredient acetophenone (CAS Reg. No. 98-86-2), and with the

List reclassification determination, as described above. I consider the one exemption established in 40 CFR part 180.920 to be reassessed for purposes of FFDCA's section 408(q) as of the date of my signature, below. A Federal Register Notice regarding this tolerance exemption reassessment decision will be published in the near future.

Lois Rossi

Lois A. Rossi, Director
Registration Division

July 7, 2006

Date

cc: Debbie Edwards, SRRD
Joe Nevola, SRRD

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MEMORANDUM

SUBJECT: Reassessment of One Exemption from the Requirement of a Tolerance for Acetophenone (CAS Reg. No. 98-86-2)

FROM: Nancy McCarroll
Toxicology Branch
Health Effects Division (7509P)

TO: Pauline Wagner, Chief
Inert Ingredient Assessment Branch (IIAB)
Registration Division (7505P)

BACKGROUND

Attached is the science assessment for acetophenone. This assessment summarizes available information on the use, physical/chemical properties, toxicological effects, exposure profile, environmental fate, and ecotoxicity of acetophenone. The purpose of this document is to reassess the existing exemption from the requirement of a tolerance for residues of acetophenone as required under the Food Quality Protection Act (FQPA).

EXECUTIVE SUMMARY

This document evaluates acetophenone, a pesticide inert ingredient of which one exemption from the requirement of a tolerance exists. An inert ingredient is defined by the U.S. Environmental Agency (USEPA) as any ingredient in a pesticide that is not intended to affect a target pest.

As an inert ingredient, acetophenone is exempt from the requirement for a tolerance when used as an attractant in pesticide formulations used on growing crops only under 40 CFR 180.920. Acetophenone is also approved for use by the U.S. Food and Drug Administration (US FDA) as a synthetic flavoring substance in food. In addition, acetophenone occurs naturally in several foods.

Acute toxicology studies indicate that acetophenone is minimally toxic via the oral or dermal routes and moderately toxic via the inhalation route. It is severely damaging

to the eye but only mildly or slightly irritating to the skin in rodents, however, it is not a dermal sensitizer in rodents. The only adverse effects noted in a short-term duration (28 days) oral study were decreased motor activity and forelimb grip and decreased food consumption at high levels (750 mg/kg). At lower doses, increased salivation was evident in both sexes. No toxicity was noted following short-term dermal exposure. Acetophenone appears more toxic via the inhalation route; however, there is low confidence in the studies supporting this statement. Acetophenone has not been tested for carcinogenicity, and it is not mutagenic in bacteria or mammalian cells. There is, however, unsubstantiated evidence of clastogenesis in cultured mammalian cells. There was no evidence of increased susceptibility to rat pups in an abbreviated rat reproduction study. Although an increased incidence of decreased pup body weight, pup survival, and live birth index was seen in the offspring, these effects occurred at levels that were three times higher than maternally toxic doses. Possible evidence of neurological significance (e.g., increased salivation, and decreased forelimb grip and motor activity) was noted in rats of a combined subchronic toxicology and reproduction/developmental toxicity study. No chronic or immunotoxicity studies were found for this compound. The main urinary metabolites of acetophenone in dogs and rabbits are 1-phenylethanol, benzoic acid and mandelic acid. Rabbits excreted an appreciable amount of 1-phenylethanol as a glucuronide conjugate.

Acetophenone readily biodegrades in the environment and the potential for bioconcentration in aquatic organisms is expected to be low. Considering acetophenone's natural presence in certain foods, its physical/chemical properties, and its fate characteristics, dietary and residential exposures of concern are not anticipated. Similarly, based on the Agency's ecotox database, acetophenone would be categorized as practically nontoxic to freshwater organisms such as plants, unicellular protozoa, invertebrates, and fish. Terrestrial risks are likely to be even lower than risks for aquatic species.

Taking into consideration all available information on acetophenone, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to acetophenone when considering exposure through food commodities and all other non-occupational sources for which there is reliable information. Therefore, it is recommended that the single exemption from the requirement of a tolerance established for residues of acetophenone when used as an attractant in pesticide formulations used on growing crops only under 40 CFR 180.920 can be considered reassessed as safe under section 408(q) of the FFDCA.

I. Introduction

This report provides a qualitative assessment for acetophenone, a pesticide inert ingredient with one tolerance exemption under 40 CFR 180.920.

II. Use Information

A. Pesticides

The tolerance exemption for acetophenone is provided in Table 1.

Table 1. Tolerance Exemption Being Reassessed in this Document

Citation as it Appears in the CFR				
40 CFR §	Tolerance Exemption Expression	Limits	Uses	CAS Registry Number and Name
180.920[a]	Acetophenone	---	Attractant	98-86-2 Acetophenone

[a] Residues listed in 40 CFR 180.920 are exempted from the requirement of a tolerance when used in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops only.

B. Other Uses

The major uses of acetophenone are as a catalyst for the polymerization of olefins; in organic synthesis, especially as a photosensitizer and as a specialty solvent for plastics and resins. It is also a chemical intermediate for the odorant ethyl methyl phenylglycidate, the riot control agent 2-chloroacetophenone, 2-bromoacetophenone for dyes, and 3-nitroacetophenone (Toxnet SIS, 2005). It is used in the manufacture of pharmaceuticals, rubber, dyestuffs, and corrosion inhibitors (Toxnet SIS, 2005).

As shown in Table 2, acetophenone is also approved for use by the U.S. Food and Drug Administration (US FDA) as a synthetic flavoring substance and adjuvant in food. It is used as a flavoring agent in non-alcoholic beverages, ice cream, candy, baked goods, gelatins, puddings, tobacco, and chewing gum. It is used to impart an orange-blossom fragrance in soaps, detergents, creams, lotions, and perfumes.

Table 2. FDA Direct Food Additive Uses for Acetophenone

Name	21 CFR §	Use Pattern
Acetophenone	172.515	Synthetic flavoring substance and adjuvants [a, b]

a. Used in the minimum quantity required to produce their intended effect, and otherwise in accordance with all the principles of good manufacturing practices.

b. Used alone or in combination with flavoring substances and adjuvants generally recognized as safe in food, prior-sanctioned for such use, or regulated by an appropriate section in this part.

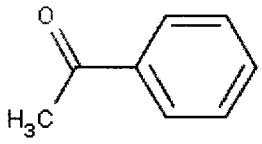
In addition, acetophenone occurs naturally in several foods (essential oil of cloves, filbert nuts, honey, nectarines, and sweet corn). It is produced as a

byproduct from the oxidation of cumene, by the oxidation of ethylbenzene and from benzene and acetylchloride in the presence of aluminum chloride, as well as catalytically from acetic and benzoic acids. Acetophenone is also a byproduct in the Hock phenol synthesis, and it is purified from the high-boiling residue by distillation.

III. Physical and Chemical Properties

Some of the physical and chemical characteristics of acetophenone's structure and nomenclature are found in Table 3.

Table 3. Physical and Chemical Properties of Acetophenone

Parameter	Value	Reference
Structure		Hazardous Substances Data Bank (HSDB) 2005
CAS # and Name	98-86-2; Acetophenone	
Empirical Formula	C_8H_8O	
Molecular Weight	120.15	
Physical State	Liquid; forms laminar crystals at low temperatures	
Melting Point	20.5° C	
Boiling Point	202° C	
Water Solubility at 25° C	6,130 mg/L	
Other Solubility	Soluble in acetone, and benzene; freely soluble in alcohol, chloroform, ether, fatty oils, and glycerol; slightly soluble in concentrated sulfuric acid	
Relative Density (water=1) at 15° C	1.1033 g/mL	
Vapor Pressure at 25° C	0.397 mm Hg	
Henry's Law Constant	1.04×10^{-5} atm m^3/mol	

IV. Hazard Assessment

Acetophenone is sponsored under EPA's High Production Volume (HPV) Challenge Program (http://www.epa.gov/chemrtk/volchall.htm). The goal of the HPV

program is to collect and make publicly available a complete set of baseline health and environmental effects data on those chemicals that are manufactured in, or imported into, the United States in amounts equal to or exceeding one million pounds per year. Industry sponsors volunteer to evaluate the adequacy of existing data and to conduct tests where needed to fill the gaps in the data, and EPA (and the public) has an opportunity to review and comment on the sponsors' robust summary report. The industry sponsor has not submitted a robust summary for acetophenone.

A. Hazard Profile

Acetophenone is being evaluated as part of the US EPA's tolerance reassessment process of inert ingredients. This assessment was developed from extracts of documents prepared by EPA's Environmental Criteria and Assessment Office, British Industrial Biological Research Association (BIBRA), USEPA Integrated Risk Information System (IRIS), International Union of Pure and Applied Chemistry (IUPAC), the Hazardous Substances Data Bank (HSDB), as well as information in the open literature.

B. Toxicological Data

Acute Toxicity

As shown in Table 4, acetophenone has minimal acute toxicity via the oral or dermal routes (Category IV). The median lethal concentration, equivalent to an LC_{50} in air for a 4-hour mouse exposure was 1.2 mg/L (IUPAC), corresponding to an air intake of 127 mg/kg (Ovchagov, 1964 as cited in EPA, 1987). This value suggests that acetophenone is moderately toxic via the inhalation route and appears to be more toxic via the inhalation rather than oral exposure. Additionally, it is severely damaging to the eye (Category I) but only mildly or slightly irritating to the skin in rodents (Category IV).

Table 4. Summary of Acute Toxicity Data for Acetophenone

Parameter	Toxicity Value/Toxicity Category	Reference
Oral LD_{50} rat	815-3,200 mg/kg/III	BIBRA, 2003
Oral LD_{50} mouse	740 mg/kg/II	
Dermal LD_{50} guinea pigs	20 g/kg IV	
Eye Irritation, rabbit [a]	Severe Irritation/I	
Skin Irritation, rabbit [b]	Mildly irritation/IV	
Dermal Sensitization, guinea pig	Not reported to be a dermal sensitizer	

a. As long as there was brief irrigation of the eyes of rabbits with water 2 minutes after instillation of undiluted acetophenone (volume not specified), there were only transient corneal effects and the eyes were normal within 24 hours. Other data, however, indicated that undiluted acetophenone caused severe damage in the rabbit eye and an "excess" of a 5% solution of acetophenone dissolved in propylene glycol was an eye irritatant (BIBRA, 2003).

b. Undiluted acetophenone was mildly irritating in rabbits 24 hours after uncovered contact with the skin. In guinea pigs, 24 hours of uncovered skin contact with 20% acetophenone was irritating at unspecified higher doses (BIBRA, 2003)

Subchronic/Chronic Toxicity

As discussed below for the study of Kapp et al. (2003), the only adverse effects noted in a short -term duration (28 days) oral study were decreased motor activity and forelimb grip and decreased food consumption at high levels (750 mg/kg). At a lower dose (225 mg/kg/day), increased salivation was evident in both sexes. No toxicity was noted following short-term dermal exposure. Acetophenone may be more toxic via the inhalation route; however, there is low confidence in the studies supporting this statement.

Oral Exposure

Acetophenone levels failed to cause reductions in body weight or any histopathologic abnormalities in the liver, kidney, spleen or testes for Sherman male rats fed diets ranging from 1-102 mg/kg/day for 30 days (Smyth, 1946 as cited in USEPA, 1987).

In a combined subchronic and reproduction/developmental screening study (Kapp et al., 2003), groups of 10 male and 10 female Sprague Dawley rats received oral gavage administrations of 0, 75, 225 or 750 mg/kg/day acetophenone for 28 days in the toxicity phase of testing. In the subchronic toxicity phase of testing, no deaths were seen; signs of overt toxicity included increased salivation at 225 and 750 mg/kg/day. The neurological examination further indicated decreased motor activity and decreased forelimb grip at 750 mg/kg/day in males only. Other signs of overt toxicity included decreased body weight and food consumption with increased cholesterol levels for the high-dose group. No effects were reported on hematological parameters. Based on these data, the LOAEL was 225 mg/kg/day (based on increased salivation in both sexes) and the NOAEL was 75 mg/kg/day. The data from females used in the reproduction/developmental phase are discussed under the Developmental and Reproductive Toxicity section of this assessment.

In a 17-week subchronic dietary study conducted by Hagan et al., 1967 (as cited in IRIS, 2003), groups of 10 male and 10 female Osborne-Mendel rats were exposed to 0, 1,000, 2,500 or 10,000 ppm

acetophenone (equivalent to 0, 50, 125, or 423 mg/kg/day)[1, 2]. No effects on growth, hematological values, or macroscopic tissue changes were seen at any dose. Similarly, there were no microscopic changes at the highest dose tested. Based on these data, IRIS (2003) concluded that the NOAEL was 423 mg/kg/day; a LOAEL was not established.

Dermal Exposure

With the exception of dermal exposure in a rat developmental study, which is discussed below, no data were found for dermal toxicity studies.

Inhalation Exposure

Two-week old rats exposed to 8.89 mg/m^3 (the method of the inhalation exposure was not specified) for 1-12 weeks showed specific patterns of mitral cell degeneration in the olfactory bulb (Pinching and Doving, 1974 as cited in USEPA, 1987). This was the only parameter measured in this study and this concentration corresponds to an uptake from air of 8.6 mg/kg/day (USEPA, 1987)[3].

In another subchronic inhalation study, groups of 15 male rats were exposed continuously to atmospheric vapors of 0, 0.007 or 0.07 mg/m^3 acetophenone for 70 days (the method of the inhalation exposure was not specified) (Imasheva, 1966 as cited in USEPA, 1987). No adverse effects were seen at the lowest concentration tested; however, rats exposed to 0.07 mg/m^3 showed cardiac vessel congestion and pronounced dystrophy of the liver. This value corresponds to a NOAEL in rats of 0.0045 mg/kg/day[3].

There is only low confidence in both of these studies because of inadequate reporting and lack of supporting data (USEPA, 1987).

Carcinogenicity

Acetophenone has not been tested for carcinogenicity. Accordingly, acetophenone cannot be classified as to human carcinogenicity.

Neurotoxicity

[1] Note: Loss of the compound from the feed was reported; therefore, the dietary concentration of 10,000 ppm was multiplied by the factor of 0.845, based on information provided by the investigators.
[2] Assuming that a rat consumes a daily amount of food equal to 5% of its body, dosages presented in ppm were converted to mg/kg/day as follows: dosage in ppm (mg/kg food) x 0.05 kg food/kg = mg/kg/day.
[3] Calculated assuming a 0.35 kg rat breathes 0.223 mg/m^3 of air/day (USEPA, 1987).

In the previously discussed combined subchronic and reproduction/ developmental oral gavage screening study abstract, adverse neurological effects were manifested as increased salivation (at 225 mg/kg/day), decreased forelimb grip strength and motor activity (at 750 mg/kg/day). These data were used to define the **neurotoxicity** NOAEL as 225 mg/kg/day and the LOAEL as 750 mg/kg/day. For females, the NOAEL is 750 mg/kg/day, based on the lack of any neurological effects; a LOAEL was not established.

Mutagenicity

Acetophenone was not mutagenic in the *Salmonella typhimurium* reverse gene mutation assay. It was also negative for the induction of gene mutations and did not produce DNA damage/repair in various strains of *Escherichia coli.* There is, however, evidence of chromosome aberration induction in hamster lung cells in the study of Sofuni et. al., as reported in BIBRA.

Developmental and Reproductive Toxicity

Oral Exposure

In the combined subchronic and reproduction/developmental oral gavage screening study, male and female rats used in the repeated dosing phase were exposed for a minimum of 28 days; these males were mated to females treated a minimum of 14 days through day 3 of lactation. There were no adverse effects on the mating or fertility indices or on gestation lengths. The live birth index was decreased at 750 mg/kg/day. Similarly, pup survival was decreased during lactation and mean pup weights were decreased at 750 mg/kg. From these findings, it was concluded that the systemic LOAEL was 225 mg/kg/day, based on increased salivation in both sexes; the NOAEL was 75 mg/kg/day. The reproductive NOAEL was 750 mg/kg/day; a reproductive LOAEL was not established. The developmental LOAEL was 750 mg/kg/day, based on decreased pup body weight, pup survival and live birth index; the NOAEL was 225 mg/kg/day (Kapp et al., 2003).

Dermal Exposure

Application of 0.48 g/kg of acetophenone to the skin of pregnant rats on days 10-15 of pregnancy did not cause adverse effects on the length of gestation, litter size, litter weight, time or appearance of teeth or hair, opening of the eyes, or appearance of reflexes (Lagno and Babhitizina, 1969, as cited in USEPA, 1987).

C. Metabolism and Pharmacokinetics

Early studies have identified 1-phenylethanol, benzoic acid and mandelic acid as urinary metabolites of acetophenone in rabbits and dogs (HSDB). Rabbits administered acetophenone by oral gavage excreted 47% of the dose as glucuronide conjugates of 1-phenylethanol and about 20% as hippuric acid. Mice appear to readily absorb acetophenone applied percutaneously (Clayton, G.D., and Clayton, F. E., as cited in HSDB).

D. Special Considerations for Infants and Children

In rat reproduction toxicology studies, effects were observed in the offspring (e.g., decreased pup body weight, pup survival and live birth index), but these effects occurred at levels that were three times higher than the maternally toxic dose. Based on this information, there is no concern, at this time, for increased sensitivity to infants and children following exposure to acetophenone used as an inert ingredient in pesticide formulations. For the same reason, a safety factor analysis has not been used to assess risk and, therefore, the additional tenfold safety factor for the protection of infants and children is also unnecessary.

V. Environmental Fate Characterization and Drinking Water Considerations

According to HSDB, acetophenone, if released to the air, will exist solely as a vapor and will be degraded in the atmosphere by reaction with photochemically produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 6 days. In soil, it is expected to have a very high mobility based on a low Koc of 10, measured in agricultural soil. Based on a Henry's Law constant of 1.04×10^{-5} atm-m^3/mol, volatilization from moist soil surfaces is expected to be moderate. If released to water, it is not expected to adsorb to suspended solids and sediment because the octanol/water partition coefficient (K_{ow} = 38) and the soil organic carbon partition coefficient (K_{oc}) indicate that the chemical is not likely to be drawn by organic matter. Furthermore, it is highly mobile and susceptible to leaching, based on the low Koc. Nevertheless, screening studies indicate that acetophenone is readily biodegradable. The biodegradation half-life is 32, 8 or 4.5 days in groundwater, river water or lake water, respectively. Volatilization from water is anticipated to be moderately rapid, based on the Henry's Law constant. Estimated volatilization half-lives for a model river and model lake were 2.5 days and 32 days, respectively. An estimated bioconcentration factor (BCF) of 0.5 suggests the potential for bioconcentration in aquatic organisms is low. Hydrolysis is not considered an important environmental fate process because this compound lacks functional

groups that hydrolyze under environmental conditions (HSDB). Acetophenone does not undergo significant direct photolysis. Considering the ready biodegradation of acetophenone, concentrations in drinking water above levels of concern are not anticipated.

VI. Exposure Assessment

As an inert ingredient, acetophenone is exempt from the requirement for a tolerance when used as an attractant in pesticide formulations used on growing crops only under 40 CFR 180.920. Acetophenone is also approved for use by the U.S. Food and Drug Administration (US FDA) as a synthetic flavoring substance in food. In addition, acetophenone occurs naturally in several foods.

Exposure to acetophenone may occur via dietary (food and drinking water) and/or residential (inhalation and dermal) pathways. Dietary exposure to residues of these chemicals would be via the oral route, by consumption of raw agricultural commodities to which pesticide products containing this chemical have been applied, and/or by consumption of drinking water. Additionally, residential exposure could occur from applications of home gardening products.

Acetophenone readily biodegrades in the environment, and the potential for bioconcentration in aquatic organisms is expected to be low. Similarly, if released to water, microbial degradation and volatilization are expected; therefore, hydrolysis, oxidation, adsorption to sediments and bioconcentration are not expected to be significant (EPA, 1987). Considering the physicals/chemical and fate properties of acetophenone, dietary and residential exposures of concern are not anticipated.

VII. Aggregate Exposures

In examining aggregate exposure, the Federal Food, Drug, and Cosmetic Act (FFDCA) section 408 directs EPA to consider available information concerning exposures from the pesticide residue in food and all other nonoccupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

For acetophenone, a qualitative assessment for all pathways of human exposure (food, drinking water, and residential) is appropriate given the lack of human health concerns associated with exposure to acetophenone as an inert ingredient in pesticide formulations.

VIII. Cumulative Exposure

Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information"

concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to acetophenone and any other substances and, this material does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that acetophenone has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

IX. Human Health Risk Characterization

As an inert ingredient, acetophenone is exempt from the requirement for a tolerance when used as an attractant in pesticide formulations used on growing crops only under 40 CFR 180.920. Acetophenone is also approved for use by the U.S. Food and Drug Administration (US FDA) as a synthetic flavoring substance in food. In addition, acetophenone occurs naturally in several foods, including clove oil, filbert nuts, honey, nectarines, and sweet corn.

Acute and subchronic toxicity studies indicate that acetophenone has is generally of low toxicity. In rat reproduction toxicology studies, no evidence of increased susceptibility was seen. Although toxicity was observed in offspring (e.g., decreased pup body weight, pup survival and live birth index) in the combined subchronic and reproduction/developmental oral study, these effects occurred at levels that were three times higher than maternally toxic dose.

Acetophenone readily biodegrades in the environment and the potential for bioconcentration in aquatic organisms is expected to be low. Considering acetophenone natural presence in certain foods, its physical/chemical properties, and its fate characteristics, dietary and residential exposures of concern are not anticipated.

Taking into consideration all available information on acetophenone, it has been determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to acetophenone when considering exposure through food commodities and all other non-occupational sources for which there is reliable information. Therefore, it is recommended that the single exemption from the requirement of a tolerance established for residues of acetophenone when used as an attractant in pesticide formulations used on growing crops only under 40 CFR 180.920 can be considered reassessed as safe under 408(q) of the FFDCA.

V. Ecotoxicity and Ecological Risk Characterization

The major routes of dissipation for acetophenone, if it is applied in agricultural settings will be leaching, metabolism and likely, volatilization. It may also be transported during rain events, via runoff, dissolved in the water, with the possibility to reach adjacent bodies of water. The chemical may reach water via spray drift. The chemical does not undergo abiotic transformation (hydrolysis, aqueous photolysis). It appears that the chemical does not linger for extended periods of time. Acetophenone does not have the potential to bioconcentrate in fish or other organisms in the water. Based on the Agency's ecotox database, acetophenone would be toxicologically categorized as practically non-toxic to freshwater organisms (fishes, plants, unicellular protozoans, and invertebrates). The Agency's Ecotox database predicted a freshwater fish LC_{50} values that ranged from 155,000-268,000 ppb. Thus, acetophenone would be categorized as practically non-toxic to freshwater fishes based on the range of LC_{50} values. Table 5 lists the toxicity data for acetophenone in reference to freshwater fish.

Table 5-Freshwater Fish Toxicity to Acetophenone

SPECIES	TOXICITY VALUE (ppb)	TOXICITY CATEGORY	REFERENCE NUMBER
Fathead minnow (*Pimephales promelas*)	LC_{50}= 155,000	Practically non-toxic	719
Fathead minnow (*Pimephales promelas*)	LC_{50}= 158,000	Practically non-toxic	719
Fathead minnow (*Pimephales promelas*)	LC_{50}= 163,000	Practically non-toxic	719
Fathead minnow (*Pimephales promelas*)	LC_{50}= 163,000	Practically non-toxic	719
Fathead minnow (*Pimephales promelas*)	LC_{50}= 164,000	Practically non-toxic	5940
Fathead minnow (*Pimephales promelas*)	LC_{50}= 162,000	Practically non-toxic	12448
Fathead minnow (*Pimephales promelas*)	LC_{50}= 208,000-268,000	Practically non-toxic	14128

For freshwater invertebrates Agency's ecotox database predicted an LC_{50} value of 162,202 ppb, making acetophenone categorized as practically non-toxic to freshwater invertebrates. Table 6 lists the toxicity data applicable to freshwater invertebrates.

Table 6-Freshwater Invertebrate Toxicity to Acetophenone

Species	Toxicity Value (ppb)	Toxicity Category	Ecotox Database Reference Number
Water flea (*Daphnia magna*)	LC50= 162,202	Practically non-toxic	16475

Although no estuarine/marine fish toxicity data was available from the Agency's ecotoxicity database, it is expected that acetophenone will exhibit similar toxicity toward estuarine/marine fishes and have a similar toxicity categorization of practically non-toxic as it does to freshwater fishes.

Despite the fact that no estuarine/marine invertebrate toxicity data were available for analysis, the Agency's ecotox databse predicts that acetophenone will be categorized as practically non-toxic to estuarine/marine invertebrates and mollusks based on the toxicity that acetophenone exhibits toward freshwater invertebrates.

Moreover, the Agency's predicted an LC_{50} value of 886,707 ppb for freshwater protozoans thus making acetophenone categorized as practically non-toxic to these organisms.

Considering the physical properties of the compound, aquatic exposures are possible. Acute effects to aquatic species (listed and non-listed) are likely if application rates exceed more than a pound per acre. Chronic effects are largely unknown. Effects due to acetophenone degradates are unknown. Terrestrial risks are likely to be lower than for aquatic species based on available mammalian data used as a surrogate for other terrestrial phase animals.

The mammalian acute LD_{50} value of 815 mg/kg categorizes acetophenone as slightly toxic to mammals. Using this as a surrogate for avian species, acetophenone may have a similar toxicity classification for birds.

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