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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DATE: **June 13, 2005**

ACTION MEMORANDUM

SUBJECT: Reassessment of One Exemption from the Requirement of a Tolerance for Acetone.

FROM: Dan Rosenblatt, Chief
Minor Use, Inerts, and Emergency Response Branch

TO: Lois A. Rossi, Director
Registration Division

I. FQPA REASSESSMENT ACTION

Action: Reassessment of one inert exemption from the requirement of a tolerance. The tolerance exemption is to be maintained.
Chemical: Acetone
CFR: 40 CFR part 180.910
CAS #: 67-64-1

Use Summary: Acetone is a highly volatile chemical that is used as an inert ingredient, a solvent/co-solvent, in a variety of pesticide products (including outdoor yard, garden, and turf products, and agricultural crop products). It is primarily used in the manufacture of other chemicals, and secondarily in the manufacture of a variety of consumer products (e.g., paints, varnishes, and automotive care products). Appreciable quantities of acetone are continually being produced in the human body as a result of the breakdown and utilization of stored fats and lipids as a source of energy.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the one exemption from the requirement of a tolerance for the inert ingredient acetone (CAS# 67-64-1). I consider the one exemption established in 40 CFR part 180.910 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 A. Rossi, Director
Registration Division

Date: June 29, 2005

CC: Debbie Edwards, SRRD
Joe Nevola, SRRD

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

June 14, 2005

MEMORANDUM

SUBJECT: Reassessment of One Exemption from the Requirement of a Tolerance for Acetone.

FROM: Karen Angulo
Minor Use, Inerts and Emergency Response Branch
Registration Division (7505C)

THRU: Pauline Wagner 6/14/05
Inerts Coordinator
Registration Division (7505C)

TO: Dan Rosenblatt, Chief
Minor Use, Inerts and Emergency Response Branch
Registration Division (7505C)

I. Background

The purpose of this document is to evaluate for reassessment the one existing exemption from the requirement of a tolerance for residues of acetone under 40 CFR §180.910 as required under the Food Quality Protection Act (FQPA) section 408. As part of the United Nations' (UN) Organization for Economic Cooperation and Development's (OECD) High Production Volume (HPV) chemical assessment program, the U.S. EPA in 1999 prepared a SIDS Initial Assessment Report (SIAR) on acetone. EPA's SIAR is being used here in lieu of a traditional inert ingredient tolerance exemption reassessment document because it provides all of the necessary human and environmental hazard and exposure information. The complete SIAR is attached. This document provides only a brief summary of SIAR's conclusions as well as conclusions for the inert ingredient reassessment.

II. Executive Summary

This report evaluates acetone, a pesticide inert ingredient that has one exemption from the requirement of a tolerance for pesticide residues when used in pesticide formulations as a solvent/co-solvent applied to growing crops or to raw agricultural commodities after harvest under 40 CFR §180.910.

Acetone is a highly volatile chemical that is used as a solvent/co-solvent in a variety of pesticide products (including outdoor yard, garden, and turf products, and agricultural crop products). It is primarily used in the manufacture of other chemicals, and secondarily in the manufacture of a variety of consumer products (e.g., paints, varnishes, and automotive care products).

Sufficient toxicity data and information on acetone are available from a variety of sources, and EPA's SIAR is being used as the basis for this assessment (the SIAR is attached). In addition, acetone has been assessed by EPA's Integrated Risk Information System (IRIS; 2003), as well as the U.S. Agency for Toxic Substances and Disease Registry (ATSDR; 1994). 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 this chemical.

The SIAR reports that the health and environmental effects of acetone have been well studied and acetone is a low priority for further work. The SIAR reports that toxicity from exposure to acetone only occurs at very high levels, therefore it has a low potential for harming either human health or the environment. In addition, appreciable quantities of acetone are continually being produced in the human body as a result of the breakdown and utilization of stored fats and lipids as a source of energy. 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. No exposure levels of concern (food, drinking water, inhalation, or dermal) are expected from the use of acetone as an inert ingredient in pesticide products.

Taking into consideration the available information on acetone, it is determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to this chemical when considering dietary exposure and all other non-occupational sources of pesticide exposure for which there is reliable information. Therefore, it is recommended that the one exemption from the requirement of a tolerance established for residues of acetone in/on raw agricultural commodities and animals can be considered reassessed as safe under section 408(q) of the FFDCA.

III. Introduction

This report evaluates the pesticide inert ingredient acetone, which has one exemption from the requirement of a tolerance when used in pesticide formulations as a solvent/co-solvent when applied to growing crops or to raw agricultural commodities after harvest under 40 CFR §180.910.

IV. Use Information

A. Pesticide Uses.

Acetone is used as a solvent/co-solvent in a variety of pesticide products, including outdoor yard, garden, and turf products, and agricultural crop products. The tolerance exemption for acetone is given in Table 1 below.

Table 1. Tolerance Exemption Being Reassessed in this Document

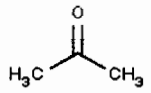
Tolerance Exemption Expression	CAS Reg No.	40 CFR §	Use (Pesticidal)
Acetone	67-64-1	180.910[1]	solvent/co-colvent

1. Residues listed in 40 CFR §180.910 are exempted from the requirement of a tolerance when used as inert ingredients in pesticide formulations when applied to growing crops or to raw agricultural commodities after harvest.

B. Other Uses.

Acetone is primarily used in the manufacture of other chemicals, and secondarily in the manufacture of a variety of consumer products (e.g., paints, varnishes, and automotive care products). Acetone has been approved by FDA as an indirect food additive.

V. Physical and Chemical Properties

Physical/Chemical	Acetone
CAS #	67-64-1
Molecular formula	C3-H6-O
Structural formula	
Molecular weight	58.08
Physical state	Liquid
Vapor Pressure	182 mm Hg at 68°F (20°C)
Flash Point	Cleveland open cup: -9°C Tag closed cup: -17°C
Water Solubility	100% at 20°C
Henry's Law constant	$1.87X10^{-5}$ atm-cu m/mole @ 25°C
Partition Coefficient (Log Kow)	-0.24

VI. Hazard Assessment

As part of OECD's HPV chemical assessment program, the U.S. EPA prepared a SIAR on acetone in 1999. Unless otherwise noted, EPA's SIAR is being used here as the basis for this inert ingredient tolerance exemption reassessment document because it provides sufficient human and environmental hazard and exposure information. Therefore, this document provides only a brief summary of the SIAR's conclusions. The complete SIAR is attached and the reader is referred to it for the full assessment.

A. Metabolism

Organs and tissues within the human body contain some acetone, and 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. The acetone found in the body is produced in the

liver following the utilization of stored fats and lipids as a source of energy. 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. 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.

B. Toxicity

Acetone's acute toxicity is low. It is not a skin irritant or sensitizer but is a defatting agent to the skin. Acetone is an eye irritant. The acute effects of a single exposure to acetone vapor in animals are generally similar to the signs of central nervous system (CNS) depression seen in cases of human intoxication. Vapor concentrations in excess of 24,000 mg/m^3 (24 mg/L) are generally required to elicit any sign of acute acetone intoxication in animals.

The subchronic toxicity of acetone has been examined in animals. The most notable findings were increased liver and kidney weights, and decreased spleen weights. Overall, the No Observed Effect Levels (NOEL) in the drinking water study were 1% for male rats (900 mg/kg/day) and male mice (2258 mg/kg/d), 2% for female mice (5945 mg/kg/day), and 5% for female rats (3100 mg/kg/day).

For developmental effects in inhalation studies, a statistically significant reduction in fetal weight, and a slight, but statistically significant increase in the percent incidence of fetal resorptions were seen at very high levels (in mice at 15,665 mg/m^3 [15.6 mg/L] and in rats at 26,100 mg/m^3 [26.1 mg/L]). The NOEL for developmental toxicity was determined to be 5220 mg/m^3 [5.2 mg/L] for both rats and mice. Teratogenic effects were not observed in rats and mice tested at 26,110 [26.1 mg/L] and 15,665 mg/m^3 [15.6 mg/L], respectively.

IRIS (2003) has concluded that the cancer data on acetone are inadequate because of limited testing in long-term cancer bioassays. Nevertheless, IRIS further states that "Acetone has a long history of industrial use as a solvent. To date there are no epidemiological studies demonstrating an association between exposure to acetone and increased risk of cancer". Both IRIS and the SIAR reported that genetic toxicology studies, which used acetone as the test material rather than the solvent, have been uniformly negative. The SIAR concluded that acetone is not carcinogenic via the dermal route of exposure.

C. Special Considerations for Infants and Children

Acetone is of low toxicity for endpoints of concern for human health effects, including developmental and reproductive effects, based on the available information. Developmental effects were only seen at very high levels. A statistically significant reduction in fetal weight, and a slight, but statistically significant increase in the percent incidence of fetal resorptions were seen at very high levels (in mice at 15,665 mg/m^3 [15.6 mg/L] and in rats at 26,100 mg/m^3 [26.1 mg/L]). The NOEL for developmental toxicity was determined to be 5220

mg/m^3 [5.2 mg/L] for both rats and mice (SIAR). Based on this available information, a safety factor analysis has not been used to assess the risks resulting from the use of acetone, therefore, an additional tenfold safety factor for the protection of infants and children is unnecessary.

VII. Environmental Fate Characterization/Drinking Water Considerations

Acetone is considered to be very volatile, with a vapor pressure of 182 mm Hg at 68°F (20°C). A substantial amount of acetone can also be found in water, which is consistent with high water solubility 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. Acetone meets the OECD definition of readily biodegradable, which requires that the biological oxygen demand is at least 70% of the theoretical oxygen demand within the 28-day test period. Acetone is rapidly biodegraded in water and this is the dominant removal process in the environment.

VIII. Exposure Assessment

For the general population, exposure to acetone can occur from using a variety of consumer products, including adhesives, paints, varnishes, cosmetics, and processed and unprocessed foods. Acetone has been approved by FDA as an indirect food additive. It can also be detected in measurable amounts in onions, grapes, cauliflower, tomatoes, milk, cheese, beans, peas, and other natural foods. Acetone is naturally produced in the human body as part of the energy production processes.

Acetone is used in a variety of pesticide products, including those for outdoor yards, gardens, turf, and agricultural crops. The high vapor pressure of acetone (182 mm Hg at 68°F [20°C]) indicates that the predominant route of exposure to the general population is through vapor inhalation. In the SIAR, an EPA modeling program entitled SCIES (Screening Consumers Inhalation Exposure Software) was used to estimate a likely indoor consumer use of a product (45 min application of a spray contact adhesive that contained 21% acetone) and predicted a short-term exposure value of 900 mg/m^3.

The volatile nature of acetone will limit the amount that will remain on food crops, and any residue that enters the body will be metabolized. In addition to volatilization from soil surfaces, acetone biodegrades readily in soil, which indicates that run-off into surface water from pesticidal uses is not expected. Therefore, dietary exposures of concern from food (including crops, meats, and fish) and drinking water are not likely from the use of acetone as an inert ingredient in pesticide products.

IV. Aggregate Exposures

In examining aggregate exposure, FFDCA section 408 directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-

occupational 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).

In developing this assessment for acetone, 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 this chemical.

X. Cumulative Exposure

Section 408(b)(2)(D)(v) of the 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 acetone and any other substances, and these materials do not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that acetone 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/

XI. Human Health Risk Characterization

Sufficient toxicity data and information on acetone are available from a variety of sources. This assessment uses the OECD SIAR report as its basis. A qualitative assessment for all pathways of human exposure (food, drinking water, and residential) is appropriate given the lack of human health concerns for acetone.

Acetone has low toxicity via all routes of exposure. It is an eye irritant, but it is not a skin irritant and does not induce sensitization. CNS and minimal developmental and teratogenic effects can result but at doses much higher than are expected to occur from pesticidal uses. Acetone is not considered to be genotoxic or carcinogenic. Acetone is very volatile and appreciable dermal exposures from pesticide use is unlikely. Inhalation exposures are expected to be below toxicity levels of concern. Acetone is produced naturally in the human body as part of the energy production processes. 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. The volatile nature of acetone and its ready biodegradation indicates that residues on food (including crops, meats, and fish) and in drinking water are unlikely.

Taking into consideration the available information on acetone, there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure when considering dietary exposure (including crops, meats, and fish) and all other non-occupational sources of pesticide exposure for which there is reliable information. Therefore, it is recommended that the one exemption from the requirement of a tolerance established for residues of acetone in/on raw agricultural commodities under 40 CFR §180.910 can be considered reassessed as safe under section 408(q) of the FFDCA.

XII. Ecotoxicity and Ecological Risk Characterization

Ecotoxicity testing shows that acetone exhibits a low order of toxicity. Acetone has been tested in a wide variety of aquatic and terrestrial species. Acute toxicity to fish ranges from an LC50 of 6,070 mg/L for Brook trout to 15,000 mg/l for Fathead minnow. The lowest LC50 for aquatic invertebrates is 2,100 mg/L, ranging to 16,700 mg/L. The NOEC's for toxicity to aquatic plants range from 5,400-7,500 mg/L. The chronic NOEC for Daphnia is 1,660 mg/L. Tests using Ring-neck pheasant and Japanese quail produced no adverse effects at 40,000 mg/kg.

References:

Acetone, Science Information Assessment Report, 1999, Organization for Economic Cooperation and Development (SIAR), (http://cs3-hq.oecd.org/scripts/hpv/)

Acetone, 2003, EPA's Integrated Risk Information System (IRIS) (http://www.epa.gov/iris/index.html)

Attachment:

Acetone, Science Information Assessment Report, 1999, Organization for Economic Cooperation and Development (SIAR), (http://cs3-hq.oecd.org/scripts/hpv/)