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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DATE: **September 6, 2005**

ACTION MEMORANDUM

SUBJECT: Inert Reassessment – Oxalic Acid (CAS Reg. No. 144-62-7)

FROM: Pauline Wagner, Chief Pauline Wagner 9/7/05
Inert Ingredient Assessment Branch

TO: Lois A. Rossi, Director
Registration Division

I. FQPA REASSESSMENT ACTION

Action: Reassessment of one inert ingredient exemption from the requirement of a tolerance. Current exemption is to be maintained.

Chemical: Oxalic Acid
CFR: 40 CFR § 180.930 formerly 40 CFR § 180.1001(e)
CAS #: 144-62-7

Table 1: Tolerance Exemption Expression

40 CFR §	Inert Ingredient	Limits	Uses (Pesticidal)
180.910	Oxalic acid (CAS Reg. No. 144-62-7)	No more oxalic acid should be used than is necessary to chelate calcium and in no case should more than 2 lb oxalic acid per acre be used.	Calcium chelating hard water inhibitor

Use Summary: Oxalic acid is used as an analytical reagent. It is also used in textile finishing; in metal, wood or equipment cleaning; in bleaching straw (hats) and leather; in removing paint, varnish, rust or ink stains; in dye manufacturing; in chemical synthesis; and in the paper, ceramics, photographic and rubber industries. In veterinary medicine, oxalic acid has also been used *in vitro* as a blood specimen anticoagulant. The active ingredient uses of oxalic acid in pesticide products were cancelled for nonpayment of fees in 1994. Oxalic acid is also used as a

calcium chelating hard water inhibitor in pesticides used in outdoor gardens and agricultural crops, at no more than necessary to chelate calcium, and at a maximum of 2 pounds per acre.

List Reclassification Determination: The current List Classification for oxalic acid is 3. Because EPA has determined that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to oxalic acid used as inert ingredients in pesticide formulations, the List Classification for oxalic acid will change from List 3 to List 4B.

II. MANAGEMENT CONCURRENCE

I concur with the reassessment of the one exemption from the requirement of a tolerance for the inert ingredient oxalic acid (CAS Reg. No. 144-62-7). I consider the one exemption established in 40 CFR § 180.910 [formerly 40 CFR § 180.1001(c)] 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

Lois A. Rossi, Director
Registration Division

Date: September 9, 2005

CC: Debbie Edwards, SRRD
Joe Nevola, SRRD

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MEMORANDUM

SUBJECT: Reassessment of One Exemption from the Requirement of a Tolerance for Oxalic Acid

FROM: R. Tracy Ward
Inert Ingredient Assessment Branch (IIAB)
Registration Division (7505C)

TO: Pauline Wagner, Chief Pauline Wagner 9/7/05
Inert Ingredient Assessment Branch (IIAB)
Registration Division (7505C)

Background

The purpose of this document is to evaluate for reassessment the one existing exemption from the requirement of a tolerance for residues of oxalic acid as required under the Food Quality Protection Act (FQPA). The U.S. EPA prepared a Reregistration Eligibility Document (RED) on oxálic acid in 1992. The RED for this inert ingredient provides the necessary human and environmental hazard and exposure information (U.S. EPA, 1992). This document provides only a brief summary of the RED's conclusions as well as conclusions for the inert ingredient reassessment.

Executive Summary

This report evaluates oxalic acid, a pesticide inert ingredient for which an exemption from the requirement of a tolerance exists for its residues when used in pesticide formulations (with no more oxalic acid than is necessary to chelate calcium, and no more than 2 lb of oxalic acid per acre) applied to growing crops or raw agricultural commodities after harvest under 40 CFR § 180.910.

Oxalic acid is an odorless, colorless powder or granular solid that is slightly soluble in water. It occurs naturally as the potassium or calcium salt in many plants and vegetables, such as spinach, Swiss chard, rhubarb and beets. Oxalic acid is also the product of the metabolism of

many molds. The chemical is a relatively strong acid, also known as ethanedioic acid, ethanedionic acid, ethane-1,2-dioic acid, or oxiric acid. Oxalic acid is used as an analytical reagent. It is also used in textile finishing; in metal, wood or equipment cleaning; in bleaching straw (hats) and leather; in removing paint, varnish, rust or ink stains; in dye manufacturing; in chemical synthesis; and in the paper, ceramics, photographic and rubber industries. In veterinary medicine, oxalic acid has also been used *in vitro* as a blood specimen anticoagulant. Oxalic acid is also used as a calcium-chelating hardwater inhibitor in pesticide formulations that are applied to growing crops or to raw agricultural commodities after harvest.

EPA's RED, generated in 1992, is being used as the basis for this assessment. The RED addresses the pesticide use of oxalic acid both as the active ingredient in disinfectants and sanitizers, and as an inert ingredient in pesticide formulations. The active ingredient uses of oxalic acid were cancelled for nonpayment of fees in 1994. The physical properties, manufacturing methods and non-pesticidal industrial uses, human health assessment (acute oral, eye, dermal, subchronic toxicity and reproductive and developmental toxicity) and environmental fate and transport sections of the RED for oxalic acid were used to develop this assessment. A recent review of available literature did not produce any new data that would change the risk conclusions of the RED, and the 1992 RED is adequate for conducting this assessment. A dietary assessment was not part of the RED, therefore, a dietary exposure analysis for the inert ingredient use of oxalic acid was conducted using the generic screening model for estimating potential oxalic acid dietary exposure and is included in this document.

Oxalic acid is corrosive, or highly irritating, to the eyes, skin and mucous membranes (including the respiratory tract). It has low to moderate acute oral toxicity, but is negative for genotoxicity in reverse mutation assays. In a multigeneration reproduction study in mice, toxic effects in pups were seen only at maternally toxic doses. Oxalic acid naturally occurs in many vegetables consumed by the general population. It biodegrades quickly in soil and surface waters, and is not expected to be present in food crops or drinking water sources at substantial concentrations. Dietary exposures to oxalic acid as a result of its pesticide use are not expected to be at levels of concern. No exposure levels of concern (food, drinking water, inhalation, or dermal) are expected from the use of oxalic acid as an inert ingredient in pesticide products.

Taking into consideration all available information on oxalic acid, it has been 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 oxalic acid when applied to growing crops or to raw agricultural commodities after harvest, can be considered reassessed as safe under section 408(q) of the Federal Food, Drug, and Cosmetic Act (FFDCA).

I. Introduction

This report evaluates the pesticide inert ingredient oxalic acid, which has one exemption from the requirement of a tolerance when used in pesticide formulations as a calcium-chelating

hard water inhibitor when applied to growing crops or to raw agricultural commodities after harvest under 40 CFR §180.910. There is sufficient information to conduct this assessment.

II. Use Information

A. Pesticide Uses

Oxalic acid is used as a calcium chelating hard water inhibitor in pesticides used in outdoor gardens and agricultural crops (Table 1). The active ingredient uses of oxalic acid were cancelled for nonpayment of fees in 1994.

Table 1. Tolerance Exemptions Being Reassessed in this Document

40 CFR § [1/]	Inert Ingredient	CAS Reg. No.	Uses (Pesticidal)	Limits
180.910	Oxalic acid	144-62-7	Calcium chelating hard water inhibitor	No more oxalic acid should be used than is necessary to chelate calcium and in no case should more than 2 lb oxalic acid per acre be used.

1. Residues listed in 40 CFR §180.910 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 or to raw agricultural commodities after harvest.

B. Other Uses

Oxalic acid is used as an analytical reagent. It is also used in textile finishing; in metal, wood or equipment cleaning; in bleaching straw (hats) and leather; in removing paint, varnish, rust or ink stains; in dye manufacturing; in chemical synthesis; and in the paper, ceramics, photographic and rubber industries. In veterinary medicine, oxalic acid has also been used *in vitro* as a blood specimen anticoagulant.

III. Physical and Chemical Properties

Table 2. Physical/Chemical Properties of Oxalic Acid (Estimated=E, Measured=M)

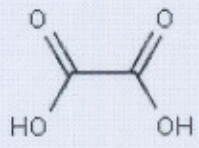
Parameter	Value	Source
Structure		NIH, 2004
Common Names	ethanedioic acid, ethanedionic acid, ethane-1,2-dioic acid or oxiric acid	NIH, 2004
CAS Reg. No.	144-62-7	

Table 2. Physical/Chemical Properties of Oxalic Acid (Estimated=E, Measured=M)		
Parameter	**Value**	**Source**
Empirical Formula	$C_2H_2O_4$	
Physical State	Odorless, colorless powder or granular solid	NIH, 2004
Molecular Weight	90.0338 (M)	NIH, 2004
Water Solubility	2.20×10^5 mg/L @ 25°C (M)	NIH, 2004
Melting Point	189.5°C (M)	NIH, 2004
Henry's Law Constant	1.43×10^{-10} atm-m3/mole @ 25°C (M)	NIH, 2004
Vapor Pressure	2.34×10^{-4} mmHg @ 25°C (M)	NIH, 2004
Octanol/Water Partition Coefficient (Log K_{ow})	-2.22 (E)	NIH, 2004

IV. Hazard Assessment

A. Hazard Profile

This hazard assessment was developed using the RED for oxalic acid prepared by the U.S. EPA in 1992. A recent review of available literature did not produce any new data that would change the risk conclusions of the RED. Unless otherwise noted, the RED is being used here as the basis for this inert ingredient reassessment document because it provides sufficient human and environmental hazard and exposure information. Therefore, this document provides a brief summary of the RED's conclusions, and additional information necessary to make the FQPA safety finding for the inert ingredient use of this chemical. The complete RED is available at http://www.epa.gov/oppsrrd1/REDs/old_reds/oxalic_acid.pdf, and the reader is referred to it for the full assessment.

B. Toxicological Data

Oxalic acid is corrosive, or very irritating, to the eyes, skin and mucous membranes (including the respiratory tract), and has an Agency classification of toxicity category I for the irritation tests. Acute oral exposure (LD_{lo} = 1000 mg/kg in dogs; LD_{50} = 300 mg/kg in gravid rats and 7500 mg/kg in rats) also causes gastric hemorrhage, central nervous system depression, convulsion, coma, and kidney damage in experimental animals.

A single subchronic toxicity study in rats fed diets with 2.5 or 5.0 percent oxalic acid (approximately 1250 to 1500, or 2500 to 3000 mg/kg/day) showed decreased body weights and restricted growth in both sexes, and disrupted estrous cycles in females. The lowest observed adverse effect level (LOAEL) was determined to be 1250 mg/kg/day. At the 2500 to 3000 mg/kg/day dose, the test animals also had reduced thyroid weights and changes in iodine and hormone levels.

A multigenerational mouse reproduction study had effects occurring at the 0.2 percent dose, or approximately 350 mg/kg/day, of oxalic acid in drinking water. Observed effects were: decreased prostate gland weights and changes in kidney weights in the parents, and abnormal sperm in males. Reduced body weight gain in dams at this dose was accompanied by decreased pup weights, number and size of litters, and number of live pups per litter. A NOAEL of 0.1 percent, or approximately 250 mg/kg/day, was established.

Gravid rats given 0, 0.18, or 0.23 mg/kg/day of oxalic acid by gavage developed renal oxalosis and gastritis, as well as slightly, but statistically significant, increased mortality. There was also a significant decrease in mean litter size, but no teratogenic effects in pups.

Reverse mutation assays using *Salmonella typhimurium* were negative for oxalic acid with and without S-9 liver fractions (Ishidate et al., 1984; Haworth et al., 1983). There was no available literature on the carcinogenicity of oxalic acid.

C. Metabolism

The 1992 RED reports that when oxalic acid is ingested by mammals, it "chelates free calcium ions and is excreted as calcium oxalate. Excess levels cause deposition of calcium oxalate in the kidney tubules and renal damage." Also, "chronic oral intake in animals produces kidney tubule damage and disturbances in calcium metabolism." Oxalic acid can form in the liver as a metabolite of ethylene glycol, which in turn is a reaction product of ethylene oxide following its application to herbs and spices.

D. Special Considerations for Infants and Children

Oxalic acid demonstrated reproductive effects only in the presence of maternal toxicity. For this reason, a safety factor analysis has not been used to assess the risks resulting from the inert ingredient use of oxalic acid in pesticidal products, and an additional tenfold safety factor for the protection of infants and children is also unnecessary.

V. Environmental Fate Characterization/Drinking Water Considerations

Oxalic acid is a solid chemical that is nonvolatile (1.43×10^{-10} atm-m3/mole @ 25° C), does not adsorb to soils and readily dissolves into surface water. Though highly soluble in water, oxalic acid forms complexes with a number of metal ions, and it is temporarily immobilized in the form of oxalate complexes and oxalate salts. Both aerobic and anaerobic conditions in soil and water biodegrade oxalic acid and its complexes in less than one day. For these reasons, oxalic acid is expected to be present in drinking water sources only at very low concentrations.

VI. Exposure Assessment

For the general population, exposure to oxalic acid can occur from consumption of foods in which it naturally occurs or from the use of a variety of consumer products, such as paints, varnishes, cleaners, and products from the paper, rubber, ceramic and photographic industries.

Oxalic acid may be released into the environment as emissions from processing/rendering of livestock by-products, tobacco smoke, automobile exhaust, pulp kraft mill effluents and by photochemical oxidations of man-made chemical compounds during long-range transport.

Oxalic acid is also used in pesticide formulations as an inert ingredient; a calcium chelator limited to no more than 2 lbs per acre. Inhalation and dermal exposures are possible from residential uses, although the use outdoors will reduce inhalation exposure. The physical properties and rapid biodegradation of oxalic acid will limit its presence in drinking water, therefore, exposure through this route is expected to be minimal. The primary route of exposure expected for the inert ingredient use of oxalic acid is through the food portion of the diet. A dietary exposure assessment for the inert ingredient use of oxalic acid was conducted by EPA using the generic screening model for estimating oxalic acid dietary exposure. Results from the Dietary Exposure Estimation Model (DEEM) are in the Dietary Risk Assessment section below.

VII. Dietary Risk Assessment for Oxalic Acid

A. Exposure Assumptions

A dietary exposure analysis for the inert ingredient use of oxalic acid was conducted using the inert ingredient dietary exposure generic screening model. This generic screening model estimates dietary exposure from all possible pre-harvest uses of pesticide products containing oxalic acid as an inert ingredient.

The dietary assessment is a bounding estimate and conservative in nature, as the screening model assumes that the inert ingredient is used on all commodities, and that 100 percent of crops are treated with the inert ingredient. Further, the model assumes finite residues for every consumed commodity (including meat, milk, poultry and eggs) in the Dietary Exposure Evaluation Model (DEEM™).

Based on the review of the oxalic acid RED, it has been determined that the subchronic toxicity endpoint of 250 mg/kg/day represents the LOAEL in the subchronic oral rat study, and it has been chosen as the point of departure for the dietary risk assessment. For the purposes of deriving a chronic population adjusted dose (cPAD), in addition to the 10x intraspecies and interspecies uncertainty factors, a 3x uncertainty factor would be applied for subchronic to chronic extrapolation. The 3x uncertainty factors for subchronic to chronic extrapolation was chosen in lieu of 10x uncertainty factors because effects seen in the study were not severe, did not significantly increase with duration of exposure, and because effects were not seen at levels below 250 mg/kg/day in the subchronic study referenced in the 1992 RED. In total, an uncertainty factor of 300 would be applied to the toxicity endpoint of 250 mg/kg/day, resulting in a cPAD of 0.833 mg/kg/day. This value is utilized in Table 3.

B. Dietary Risk from Food

Table 3 provides a summary of the results of the chronic dietary risk estimates for oxalic acid. The estimated exposure for the total U.S. population is less than 15 % of the cPAD, with

children ages 1-2 being the highest exposed population with exposures calculated at 50% of the cPAD. These exposure levels are not of concern to the Agency.

This dietary assessment includes the existing use of oxalic acid as a pesticide inert ingredient used on growing crops and raw agricultural commodities after harvest under 40 CFR § 180.910, limited to no more oxalic acid than is necessary to chelate calcium and a maximum of 2 lbs. per acre. The screening model for estimating dietary exposure assumes that pre-harvest applications treat 100 percent of all crops. A post-harvest application to agricultural commodities would have the same assumptions (including the 2 lbs. per acre limit). Therefore, a post-harvest application of oxalic acid, with or without pre-harvest application, would not be expected to increase dietary exposures above levels of concern. Dietary exposures of concern from food are not likely from the use of oxalic acid as an inert ingredient in pesticide products.

Table 3. Chronic Dietary (Food) Risk Estimates for Oxalic Acid

Population Subgroup	Oxalic Acid Estimated Exposure, mg/kg/day	% cPAD1[1]
U.S. Population (total)	0.12	14.4
All infants (< 1 year)	0.25	30.0
Children (1-2 years)	0.42	50.4
Children (3-5 years)	0.31	37.2
Children (6-12 years)	0.18	21.6
Youth (13-19 years)	0.10	12.0
Adults (20-49 years)	0.085	10.2
Adults (50+ years)	0.085	10.2
Females (13-49 years)	0.085	10.2

1. cPAD=0.833 mg/kg/day

VIII. Aggregate Exposure

In examining aggregate exposure, 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).

Oxalic acid is a metabolite of ethylene glycol, which is a metabolite of ethylene oxide. In assessing the aggregate exposure to oxalic acid, the residues of ethylene glycol and ethylene oxide must also be considered. The Agency expects that the food uses of ethylene oxide will result in insignificant exposure to drinking water resources. Ethylene oxide does not persist in the environment because it is reactive and degrades by biotic and abiotic processes. Ethylene glycol also breaks down rapidly in air, soils and water, and is not expected to accumulate in the environment or foodstuffs. Therefore, these metabolites are not expected to contribute significantly to aggregate exposure.

For oxalic acid, a qualitative assessment for human exposures from drinking water and residential use is appropriate given the lack of human health concerns associated with these types of exposures to oxalic acid because of its physical properties and the small amount of this chemical used in pesticide formulations. However, the conservative screening model assessment for dietary exposure described above is also necessary, because of the toxicity observed in acute and subchronic toxicity studies.

IX. 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 oxalic acid 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 oxalic acid 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.

X. Human Health Risk Characterization

Oxalic acid is corrosive, or highly irritating, to the eyes, skin and mucous membranes (including the respiratory tract). It has low to moderate acute oral toxicity, but is negative for genotoxicity in reverse mutation assays. In a multigeneration reproduction study in mice, toxic effects in pups were seen only at maternally toxic doses.

Oxalic acid naturally occurs in many vegetables consumed by the general population. It biodegrades quickly in soil and surface waters, and is not expected to be present in food crops or drinking water sources at substantial concentrations. Dietary exposures to oxalic acid as a result of its pesticide use are not expected to be at levels of concern.

Typically, less than 1% to 2% of oxalic acid is used as a calcium chelator in pesticide products. End-use products that contain oxalic acid bear caution statements on the labels to indicate moderate dermal and eye irritation. Based on this caution statement, product labeling requires the use of personal protective equipment (PPE). Inhalation exposures are not expected because oxalic acid is nonvolatile (1.43×10^{-10} atm-m3/mole @ 25°C).

Taking into consideration all available information on oxalic acid, 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 oxalic acid on growing crops and raw agricultural commodities after harvest under 40 CFR §180.910 can be considered reassessed as safe under section 408(q) of the FFDCA.

XI. Ecotoxicity and Ecological Risk Characterization

A small amount of oxalic acid is used as an inert ingredient in pesticide formulations. Due to its quick aerobic and anaerobic biodegradability, the oxalic acid residues that leach from the soil into water are not expected to pose a risk concern, especially to nontarget plant and animal species. A structural activity report (SAR) indicates that the chemical is practically non-toxic to all aquatic organisms with effects concentrations exceeding 1000 ppm across all taxa. Based on the endangered species level of concern, applications would need to be > 100 pounds per acre to result in the potential for risks. Based on the maximum application rate of 2 pounds per acre, no effects are likely.

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