The following information was generated from the
Hazardous Substances Data Bank (HSDB),
a database of the National Library of Medicine's TOXNET system
(http://toxnet.nlm.nih.gov) on May 21, 2009.

Query: Records containing the term 77 92 9

1
NAME: CITRIC ACID

HSN: 911

RN: 77-92-9

HUMAN HEALTH EFFECTS:

HUMAN TOXICITY EXCERPTS:

/HUMAN EXPOSURE STUDIES/ While presumably aqueous solutions (2% in one case, not stated in the other) may produce pain or "sting", patch testing of 60 eczema patients with 2.5% citric acid in petrolatum did not produce any irritant or allergic reactions; thus, the reaction appears to reflect mainly the acid effect of the substance... [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/HUMAN EXPOSURE STUDIES/ Repeated exposure of up to 15 g/d of potassium and sodium citrate as medications did not cause any reported marked side effects, but minor gastrointestinal disturbances (diarrhea, indigestion, nausea, "burning") were experienced by 22 out of 81 patients taking potassium citrate in water and 7 out of 75 taking solid potassium citrate (doses not stated in both groups) for the treatment of renal calculi. /Potassium and Sodium Citrates/ [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/SIGNS AND SYMPTOMS/ Injection of large volumes of citrated blood during transfusion may lead to hypocalcaemia and changes in blood composition with concomitant nausea, muscle weakness, breathing difficulties and even cardiac arrest. [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/SIGNS AND SYMPTOMS/ ... Within a concentration range of 0.625-320.0 mg/ml, inhaled citric acid caused cough in all subjects. Geometric mean (range) cough threshold was 13 (2.5-160) in normal subjects, 14 (5-40) in patients with mild, and 32 (20-40) mg/ml in patients with moderate to severe asthma, 40 (20-80) in current smokers, and 119 (80-160) in occasional smokers. [Schmidt D et al; Eur J Med Res 2 (9): 384-8 (1997) ]**PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=PubMed" target=new>PubMed Abstract

/SIGNS AND SYMPTOMS/ Citric acid is generally considered innocuous, although hypocalcemic effects were reported during transfusion of large volumes of citrated blood ... Frequent or excessive intake of citric acid may cause erosion of teeth and local irritation of mucous membranes. This effect also occurs with lemon juice, which contains about 7% citric acid and has a pH < 3. [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:768]**PEER REVIEWED**

/CASE REPORTS/ In one patient a splash of large quantity of saturated solution of citric acid in eyes caused severe conjunctival reaction & ulceration of cornea, resulting in extensive adherent leukoma. [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 242]**PEER REVIEWED**

/CASE REPORTS/ Two patients who suffered cardiac arrests after dialysis using hypertonic citrate are discussed. Both received anticoagulation as described in the literature, although the citrate infusion rate was lower than recommended. EKG obtained during the first such session showed no change in the Q-Tc interval with initiation of the infusion in either patient. Both were noted to have cardiac arrest within 5 minutes of discontinuation of dialysis, without warning symptoms, following the second and fifteenth treatments, respectively. The initial rhythm of ventricular fibrillation did not respond to standard advanced cardiac life support therapy, and the patients were not successfully resuscitated until they received intravenous calcium. It was postulated that the loss of positive calcium flux from the dialysate, in conjunction with circulating unmetabolized citrate, caused an electrolyte imbalance leading to the potentially fatal arrhythmia. Caution is recommended in using this method of regional anticoagulation. /Citrate/ [Charney DI, Salmond R; Asaio Trans 36 (3): M217-9 (1990) ]**PEER REVIEWED**

/CASE REPORTS/ After ingesting a single dose of 25 g citric acid (approx. 417 mg/kg) a young woman vomited and almost died. [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/CASE REPORTS/ ... ingestion of a massive oral citric acid load included metabolic acidosis accompanied by an increase in the plasma anion gap that was not caused by L -lactic acidosis, hyperkalemia, and the abrupt onset of hypotension. [DeMars CS et al; Ann Emerg Med 38 (5): 588-91 (2001) ]**PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed" target=new>PubMed Abstract

/ALTERNATIVE and IN VITRO TESTS/ ... incubation of cultured human dental pulp cells in medium containing 0.5% (pH 4.74) or 1.0% (pH 3.42) of citric acid for 2 h lead to 25% and 48% of cell death, respectively. Cytotoxicity of citric acid was associated with its acidity. Exposure of cells to pure 1% citric acid (pH 2.26) for 60 s lead to immediate cell death. Cytotoxicity was usually preceded by cell retraction, cell surface blebbing, and finally uptake of trypan blue. A medium containing 0.05% citric acid can retard the growth of pulp cells. [Chan CP et al; J Endod 25 (5): 354-8 (1999) ]**PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed" target=new>PubMed Abstract

/OTHER TOXICITY INFORMATION/ The erosive action of buffered and unbuffered aspirin (acetylsalicylic acid) on dental enamel was compared in vitro with that of citric acid and a cola soft drink. The degree of erosion depended on the duration of exposure and the concn of the acidic agent used. The unbuffered acetylsalicylic acid caused a slightly lower degree of erosive changes of enamel surfaces than citric acid. Calcium carbonate as buffer completely prevented erosion of the dental enamel induced by acetylsalicylic acid. [Hannig M et al; Drug Invest 4 (6): 484-91 (1992) ]**PEER REVIEWED**

SKIN, EYE AND RESPIRATORY IRRITATIONS:

Inhalation of dust irritates nose and throat. Contact with eyes causes irritation. [U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5., p. ]**PEER REVIEWED**

DRUG WARNINGS:

A study of abdominal pain and severity of other side effects attributed to Picolax, a combination of citric acid, magnesium oxide and sodium picosulfate, was conducted among 267 patients, 55 of whom had inflammatory bowel disease, all of whom were given a full single dose of Picolax as preparation for radiology or endoscopy. The frequency of increased abdominal pain and severe side effects after Picolax administration was similar in the patients with inflammatory bowel disease and the patients with other colonic disorders. None of the patients with iron deficiency in whom investigations had yielded negative results reported severe side effects; this was significantly different from the proportion reporting severe side effects among the patients with inflammatory bowel disease,

the irritable bowel syndrome and diverticular disease. The increase in the mean number of stools/24 hr after Picolax was lower in the patients with inflammatory bowel disease than in the other diagnostic groups. On review 2-4 wk after examination none of the patients with inflammatory bowel disease reported deterioration in their symptoms. [McDonagh AJ et al; Br Med J 299: 776-7 (1989) ]**PEER REVIEWED**

Following the occurrence of aluminum encephalopathy in four patients with chronic renal failure, 34 azotemic patients seen during the same year and five volunteers who took varying combinations of aluminum hydroxide and an alkalinizing citrate (Shohl's) solution were studied. It was found that the four encephalopathic cases were older than the 34 azotemic patients (68 years + or - 14 standard deviation, versus 50 + or - 13, p < 0.05), had a higher mean serum aluminum value (727 ug/l + or - 320 versus 92 + or - 73, p < 0.005), had taken more aluminum hydroxide (5 g/day + or - 0.9 versus 1.6 + or - 1.8, p < 0.01), and more Shohl's solution (64 ml/day + or - 19 versus 20 + or - 29, p < 0.01). In all 38 patients the serum aluminum values correlated directly with age (p= 0.01), aluminum hydroxide (p= 0.001) and concomitant citrate intake (p= 0.004). In the five healthy volunteers the 24 hr urinary aluminum excretion increased from a baseline of 22 ug + or - 19 standard deviation to 167 + or - 109 (p= 0.05) during aluminum hydroxide intake, rising to 580 + or - 267 (p= 0.01) during the simultaneous intake of citrate and aluminum hydroxide. Corresponding serum aluminum values were 11 ug/l + or - 2 standard deviation, 44 + or - 34 (p= 0.1), and 98 + or - 58 (p < 0.05). Thus citrate seems to enhance aluminum absorption and may cause encephalopathy in patients with chronic renal failure, especially the elderly.[Bakir AA et al; Clin Nephrol 31 (1): 40-4 (1989)]**PEER REVIEWED**

PROBABLE ROUTES OF HUMAN EXPOSURE:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,691,218 workers (1,083,005 of these are female) are potentially exposed to citric acid in the US(1). Occupational exposure to citric acid may occur through dermal contact with this compound at workplaces where citric acid is produced or used(SRC). Monitoring data indicate that the general population may be exposed to citric acid via ingestion of food and dermal contact with this compound and other products containing citric acid(SRC). [(1) NIOSH; International Safety Cards. Citric Acid. 77-92-9. Available at http//www.cdc.gov/niosh/ipcs/nicstart.html as of April 26, 2006. ]**PEER REVIEWED**

BODY BURDEN:

Citric acid was found to be excreted by humans through urine at a rate of 3-17 mg/kg body weight/day and through sweat at 0.2 mg/100 ml(1). [(1) Verschueren K; Handbook of Environmental Data on Organic Chemicals, Vol 1-2, 4th ed. John Wiley and Sons; New York, NY (2001) ]**PEER REVIEWED**

EMERGENCY MEDICAL TREATMENT:

EMERGENCY MEDICAL TREATMENT:

EMT COPYRIGHT DISCLAIMER:
<p>The following Overview, *** CITRIC ACID ***, is relevant for this HSDB record chemical.

LIFE SUPPORT:

- This overview assumes that basic life support measures have been instituted.

CLINICAL EFFECTS:

0.2.1 SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

A) ACUTE - A moderately strong acid with irritant and allergenic properties. It is generally considered harmless except in large ingestions or chronic exposure.

1) INGESTION - Severe metabolic acidosis, hyperkalemia, hypotension and tachycardia have been reported in a case of significant citric acid ingestion.
2) EYE - May be a severe irritant.
3) SKIN - A moderate skin irritant.
4) INJECTION - Poisonous IV, moderately toxic when given intraperitoneally, or subcutaneously.

0.2.1.2 CHRONIC EXPOSURE

A) RABBITS fed 7.7% sodium citrate (5% free acid equivalent) for 150 days developed no gross or histopathological changes, no growth differences, and no differences in survival (Clayton & Clayton, 1994).

B) RATS fed 1.2 percent citric acid for 90 weeks experienced no harmful effects on growth, reproduction, blood values, pathology, or calcium levels. Slight dental attrition was seen (Clayton & Clayton, 1994).

C) DOGS given 1,380 mg/kg citric acid daily for 112 to 120 days did not develop renal damage (Clayton & Clayton, 1994)

D) MICE given 5% citric acid in the diet had normal food intake, but loss in body weight and reduced survival time Litter size or survival up to weaning of the young mice were not effected (Clayton & Clayton, 1994).

0.2.4 HEENT

0.2.4.1 ACUTE EXPOSURE

A) Chronic ingestion may cause tooth erosion and local irritation

B) EYES - A splash of a saturated citric acid solution caused severe conjunctival reaction and corneal ulceration.

1) Animals, a single drop of 2 to 5% did not produce significant injury but irrigation for 30 minutes caused severe damage. Application of 750 micrograms to rabbit eyes produced severe irritation

C) Citric acid dust may also irritate the nose and throat.

0.2.5 CARDIOVASCULAR

0.2.5.1 ACUTE EXPOSURE

A) Hypotension and tachycardia have been reported in a case of significant citric acid ingestion.

0.2.6 RESPIRATORY

0.2.6.1 ACUTE EXPOSURE

A) Fatally poisoned animals developed cyanosis.

0.2.7 NEUROLOGIC

0.2.7.1 ACUTE EXPOSURE

A) Fatally poisoned rabbits and rats developed convulsions.

0.2.8 GASTROINTESTINAL

0.2.8.1 ACUTE EXPOSURE

A) May occasionally be a gastrointestinal irritant. Sodium citrate and citric acid solutions has direct irritating effect on oral mucous membranes and may cause necrotic and ulcerative lesions.

0.2.11 ACID-BASE

0.2.11.1 ACUTE EXPOSURE

A) Severe metabolic acidosis has been reported in a case of significant citric acid ingestion.

0.2.12 FLUID-ELECTROLYTE

0.2.12.1 ACUTE EXPOSURE

A) Hyperkalemia was reported in a patient after ingesting a large volume of citric acid.

B) Transfusion with large amounts of citrated blood has produced hypocalcemia.

0.2.14 DERMATOLOGIC

0.2.14.1 ACUTE EXPOSURE

A) Moderate irritation has been observed in animals after applications for 24 hours.

0.2.15 MUSCULOSKELETAL

0.2.15.1 ACUTE EXPOSURE

A) Fatally poisoned rabbits developed muscle contractions or spasticity.

0.2.19 IMMUNOLOGIC

0.2.19.1 ACUTE EXPOSURE

A) It has been reported to have allergenic properties

0.2.20 REPRODUCTIVE HAZARDS

A) Not shown to be a reproductive hazard.

0.2.21 CARCINOGENICITY

0.2.21.1 IARC CATEGORY

A) IARC Carcinogenicity Ratings for CAS77-92-9 (IARC, 2004):

1) Not Listed

0.2.21.2 HUMAN OVERVIEW

A) At the time of this review, no data were available to assess the carcinogenic potential of this agent.

0.2.22 GENOTOXICITY

A) At the time of this review, no data were available to assess the mutagenic or genotoxic potential of this agent.

LABORATORY:

A) Institute continuous cardiac monitoring and obtain an ECG.

B) Monitor vital signs, including pulse and blood pressure after significant citric acid overdose.

C) Monitor potassium and ionized calcium levels after significant citric acid overdose.

D) Obtain an arterial blood gas in symptomatic patients and follow until acid/base abnormalities are improving.

TREATMENT OVERVIEW:

0.4.2 ORAL EXPOSURE

A) Citric acid is not highly toxic and GI decontamination and treatment is seldom necessary.

B) Monitor serum potassium and ionized calcium concentration in symptomatic patients or in patients who have acutely ingested large amounts.

C) Treat severe hyperkalemia (associated dysrhythmias, QRS widening) aggressively. Monitor ECG continuously during and after therapy.

1) Calcium chloride: Adult: 5 ml IV bolus of a 10% solution over 5 minutes; Child: 0.2 to 0.3 milliliters/kilogram of a 10% solution over 5 to 10 minutes (20 to 30 milligrams/kilogram/dose)

2) Sodium bicarbonate: Adult or Child: 1-2 mEq/kilogram IV bolus

3) Insulin/dextrose: Adult: 5 to 10 units regular insulin IV bolus with 100 milliliters of D50 IV immediately; monitor serum glucose every 30 minutes. Child: 0.5 to 1 gram/kilogram dextrose as D25 or D10 IV followed by 1 unit of regular insulin for every 4 grams of dextrose infused; monitor serum glucose every 30 minutes.

D) HYPOTENSION: Infuse 10 to 20 mL/kg isotonic fluid. If hypotension persists, administer dopamine (5 to 20 mcg/kg/min) or norepinephrine (ADULT: begin infusion at 0.5 to 1 mcg/min; CHILD: begin infusion at 0.1 mcg/kg/min); titrate to desired response.

E) Administer intravenous calcium in patients with laboratory or ECG evidence of hypocalcemia.

0.4.3 INHALATION EXPOSURE

A) INHALATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty breathing develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer oxygen and assist ventilation as required. Treat bronchospasm with inhaled beta2 agonist and oral or parenteral corticosteroids.

0.4.4 EYE EXPOSURE

A) DECONTAMINATION: Irrigate exposed eyes with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

0.4.5 DERMAL EXPOSURE

A) OVERVIEW

1) DECONTAMINATION: Remove contaminated clothing and wash exposed area thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.

RANGE OF TOXICITY:

A) Minimum lethal human exposure is unknown.

B) Severe metabolic acidosis, hyperkalemia, hypotension and tachycardia have been reported in a case of significant citric acid (530 g/L) ingestion (elevated citrate level of 20 mEq/L on admission).

ANTIDOTE AND EMERGENCY TREATMENT:

/SRP:/ Basic treatment: Establish a patent airway (oropharyngeal or nasopharyngeal airway, if needed). Suction if necessary. Watch for signs of respiratory insufficiency and assist respirations if necessary. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary ... . Monitor for shock and treat if necessary ... . For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with 0.9% saline (NS) during transport ... . Do not use emetics. For ingestion, rinse mouth and

administer 5 ml/kg up to 200 ml of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool. Activated charcoal is not effective ... . Do not attempt to neutralize because of exothermic reaction. Cover skin burns with dry, sterile dressings after decontamination ... . /Organic acids and related compounds/ [Currance, P.L. Clements, B., Bronstein, A.C. (Eds).; Emergency Care For Hazardous Materials Exposure. 3Rd edition, Elsevier Mosby, St. Louis, MO 2005, p. 176-7]**PEER REVIEWED**

/SRP:/ Advanced treatment: Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious, has severe pulmonary edema, or is in severe respiratory distress. Early intubation, at the first sign of upper airway obstruction, may be necessary. Positive-pressure ventilation techniques with a bag valve mask device may be beneficial. Consider drug therapy for pulmonary edema ... . Consider administering a beta agonist such as albuterol for severe bronchospasm ... . Monitor cardiac rhythm and treat arrhythmias as necessary ... . Start IV administration of D5W /SRP: "To keep open", minimal flow rate/. Use 0.9% saline (NS) or lactated Ringer's (LR) if signs of hypovolemia are present. For hypotension with signs of hypovolemia, administer fluid cautiously. Consider vasopressors if patient is hypotensive with a normal fluid volume. Watch for signs of fluid overload ... . Use proparacaine hydrochloride to assist eye irrigation ... . /Organic acids and related compounds/ [Currance, P.L. Clements, B., Bronstein, A.C. (Eds).; Emergency Care For Hazardous Materials Exposure. 3Rd edition, Elsevier Mosby, St. Louis, MO 2005, p. 177]**PEER REVIEWED**

ANIMAL TOXICITY STUDIES:

NON-HUMAN TOXICITY EXCERPTS:

/LABORATORY ANIMALS: Acute Exposure/ Coughing is reported for guinea pigs exposed for 30 minutes to atmospheric citric acid concentrations of 81 mg/cu m (aerosolised 6% solution). Coughing was also produced in guinea pigs exposed to 75 mg citric acid/mL as an aerosol for 3 minutes. ...Coughing was also caused by instillation of 1 mL of an approx. 5.2% solution to the lower trachea in lambs, but not by instillation to the mid-trachea or laryngeal area. [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ The application of a 50% citric acid solution to the tongue of dogs for 5 minutes resulted in severe ulceration and tissue damage. [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006:

http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ ... Acute administration of citric-acid /to mice and rats by oral, subcutaneous, and intraperitoneal administration/ resulted in ataxia, other motor changes, and death caused by respiratory or cardiac failure. Median lethal dose values for citric-acid were similar to those for commercial citric-acid. ... Subacute administration resulted in normal behavior and no significant hematological changes. Increased protein was seen in the urine and a decrease was seen in plasma protein, albumin, and cholesterol. Histopathology revealed no specific deleterious effects of citric-acid on the organs and tissues studied. [Yokotani H et al; J Takeda Res Laboratories 30 (1): 25-31 (1971) ]**PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ ... Citric acid and malic acid caused 71% and 43% fall in Mean Arterial Blood Pressure (MABP) of rats at the doses of 15 mg/kg and 30 mg/kg respectively while pyridine hydrochloride produced 34% rise in the MABP of rats at the dose of 30 mg/kg. LD50 and LD100 of citric acid in mice have been determined as 545 mg/kg and 1000 mg/kg, respectively. [Saleem R et al; Arch Pharm Res 27 (10): 1037-42 (2004) ]**PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed" target=new>PubMed Abstract

/LABORATORY ANIMALS: Acute Exposure/ Citric acid has a low acute toxicity by oral application in both rat and mouse. General effects comprised physiological disturbances (acidosis and calcium deficiency), while "high" doses caused nervous system effects as well as severe damage to the stomach mucosa. [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Citric acid tested on rabbit eyes as single drop of 2% to 5% solution in water caused little or no injury ... Irrigation for 30 min with 0.5% to 2% solution causes severe injury; the 0.5% solution causes permanent cloudiness of cornea, and the 2% solution causes severe dense opacification. [Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 242]**PEER REVIEWED**

/LABORATORY ANIMALS: Acute Exposure/ Application of 500 mg citric acid to rabbit skin produced moderate irritation in 24 hr, whereas 750 mg caused severe irritation in the rabbit eye. [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:767]**PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Citric acid

(sodium salt) at 7.7% (equivalent to 5% free acid) in the diet of rabbits for 150 days produced no gross or histopathological changes or differences in growth or survival. /Citric acid, sodium salt/ [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:767]**PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ In dogs, a daily oral dose of 1380 mg/kg for 112 to 120 days produced no evidence of renal damage. [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:767]**PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ Groups of 10 male rats being fed up to 4.8% citric acid in feed (corresponding to approximately 4.67 g/kg/d) for 6 weeks showed slight growth reduction and, in the highest-dose group, mild blood and urine parameter changes and slight degeneration of the thymus gland and spleen. [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/LABORATORY ANIMALS: Subchronic or Prechronic Exposure/ In guinea pigs fed 1-5% citric acid (approx. 0.4- 2 g/kg/d) for 60 days, a reduced packed cell volume in the blood was the only effect noted. [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ A 2-year chronic oral study in rats being given 5% or 3% citric acid in feed (approx. 2 resp. 1.2 g/kg/d) found slightly decreased growth in the higher dosage group but no tissue abnormalities in the major organs. From the lower dosage a NOAEL of 1200 mg/kg/d results. Similarly, NOAELs of 1500 mg/kg/d (rabbit) and of 1400 mg/kg/d (dog) have been determined. [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ ... The effect of citric acid on the survival time of immature and sexually mature male mice and on the survival time and reproductive capacity of rats and mice /was studied/. Citric acid (5% in the diet) did not depress food intake but caused a loss in body weight gain and reduced survival time in mice and a slightly greater influence on mature animals. No effect was detected on the litter size or survival up to weaning of young mice or rats. The effects on body weight gain and survival time may have resulted from the chelating ability of citric acid, which could impair absorption of calcium and iron. [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's

Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:768]**PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ In a two-generation 90 days study with male and female rats fed 1.2 % citric acid no adverse effect on reproductive parameters nor any teratogenicity of dietary citric acid was seen. There were no indications of teratogenic or other adverse effects in three shorterterm reproductive studies in rats with dietary dosage of either 5% citric acid (approx. 2.5 g/kg/d) previous, during and after mating (NOEL = 2500 mg/kg/d), or 295 mg/kg/d (route unspecified) during days 6-15 of pregnancy. [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ ... Findings of no effects were reported for two reproductive and teratogenicity studies in mice receiving either 5 % citric acid (approx. 7.5 g/kg/d; in the range of acute LD50) previous, during and after mating (NOEL = 7500 mg/kg/d) or 241 mg/kg/d during days 6 - 15 of pregnancy. [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ ...There were no indications of teratogenicity or other adverse effects in female hamsters receiving 272 mg citric acid/kg during days 6-10 of pregnancy nor in female rabbits receiving up to 425 mg/kg/d during days 6-18 (NOEL = 425 mg/kg/d). [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/GENOTOXICITY/ A dominant lethal assay with male rats being treated with up to 3 g/kg/d for 5 days was negative; no chromosomal damage occurred in the bone marrow cell of these male rats. [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

/GENOTOXICITY/ ... Citric acid did not induce mutations at concentrations up to 5 mg/plate in Salmonella typhimurium strains TA 92, TA 94, TA 98, TA 100, or TA 1535, and TA 1537 with or without a liver homogenate from rats pretreated with the polychlorinated biphenyl KC-400, and no clastogenic effects were seen in Chinese hamster fibroblast cells at concentrations up to 1 mg/mL. [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:768]**PEER REVIEWED**

ECOTOXICITY EXCERPTS:

/OTHER TERRESTRIAL SPECIES/ The entomopathogenic fungus, Beauveria bassiana, produced citric acids in liquid cultures containing grasshopper (Melanoplus sanguinipes) cuticle as the sole nutrient source. Citric acids solubilized cuticular proteins as well as commercial preparations of elastin and collagen. Melanoplus sanguinipes treated with Beauveria bassiana showed a LT50 of 7.33 days, while Melanoplus sanguinipes treated with citric acid showed a LT50 of 7.25 and 13.28 days, respectively. Melanoplus sanguinipes treated with citric acid followed by a Beauveria bassiana conidia treatment showed a LT50 of 3.88 days. Analysis of the bioassay data revealed that the relationship between citric acid together with Beauveria bassiana conidia in grasshopper mortality was markedly synergistic. It is suggested that acid metabolites produced by Beauveria bassiana may play a role in cuticle solubilization and subsequent hyphal penetration. [Bidochka MJ, Khachatourians GG; J Invertebr Pathol 58 (1): 106-17 (1991) ]**PEER REVIEWED**

NON-HUMAN TOXICITY VALUES:

LD50 Rat oral 6730 mg/kg [Milne, G.W.A. Veterinary Drugs: Synonyms and Properties. Ashgate Publishing Limited, Aldershot, Hampshire, England 2002., p. 155]**PEER REVIEWED**

LD50 Rat ip 975 mg/kg /monohydrate/ [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 406]**PEER REVIEWED**

LD50 Mouse iv 42 mg/kg /From table/ [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:751]**PEER REVIEWED**

LD50 Mouse oral 5040 mg/kg /From table/ [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:751]**PEER REVIEWED**

LD50 Mouse ip 903 mg/kg /From table/ [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:751]**PEER REVIEWED**

LD50 Mouse sc 2700 mg/kg /From table/ [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:751]**PEER REVIEWED**

LD50 Rat ip 883 mg/kg /From table/ [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:751]**PEER REVIEWED**

LD50 Rat sc 5500 mg/kg /From table/ [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:751]**PEER REVIEWED**

LD50 Rabbit iv 330 mg/kg /From table/ [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:751]**PEER REVIEWED**

ECOTOXICITY VALUES:

LC50 Carcinus maenas (Green or European shore crab) 160 mg/L/48 hr; renewal /formulated product/ [Portmann JE, Wilson KW; Shellfish Information Leaflet No.22 (2nd ed) Ministry of Agric Fish Food:12 (1971) as cited in the ECOTOX database: http://mountain.epa.gov/cgi-bin/ecotox_quick_search as of April 20, 2006. ]**PEER REVIEWED**

METABOLISM/PHARMACOKINETICS:

METABOLISM/METABOLITES:

Citric acid is a normal metabolite and an intermediate in cellular oxidative metabolism ... The acid is formed in the mitochondrion after condensation of acetate with oxaloacetate. The six-carbon acid is then successively degraded to a series of four-carbon acids, effectively accomplishing oxidation of acetate in the cell. [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:767]**PEER REVIEWED**

In human (as well as in animal and plant) physiology, citric acid is a very common intermediate in one of the central biochemical cycles, the Krebs or tricarboxylic acid cycle, which takes place in every cell. It completes the breakdown of pyruvate formed from glucose through glycolysis, thereby liberating carbon dioxide and a further four hydrogen atoms which are picked up by electron transport molecules. Thus, in man approximately 2 kg of citric acid are formed and metabolised every day. This physiological pathway is very well developed and capable of processing very high amounts of citric acid as long as it occurs in low concentrations. [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 2001). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

Citric acid in reaction with enzyme citratase /citrate lyase/ yields oxaloacetic acid & acetic acid. [Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975., p. 785]**PEER REVIEWED**

ABSORPTION, DISTRIBUTION & EXCRETION:
/A portion/ of the circulating (mainly metabolic but also ingested) citric acid is excreted in urine, with 24-hour urine reference values between 1.5 and 3.68 mmol, corresponding to 0.29-0.71 g citric acid excreted per person per day. [United Nations Environment Programme: OECD; Screening Information Data Sheets on Citric Acid (77-92-9) (January 1997). Available from, as of May 9, 2006: http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html]**PEER REVIEWED**

MECHANISM OF ACTION:
... The NK(2), and to a lesser extent the NK(1), receptors have been shown to be involved with citric acid-induced bronchoconstriction in the guinea pig, which is in part mediated by endogenously released bradykinin. Tachykinins and bradykinin could also modulate citric acid-induced bronchoconstriction. ... Bronchoconstriction induced by citric acid inhalation in the guinea pig, mainly caused by the tachykinin NK(2) receptor, is counteracted by bronchoprotective NO after activation of bradykinin B(2) and tachykinin NK(1) receptors in airway epithelium. [Ricciardolo FL; Am J Med 111 (Suppl 8A): 18S-24S (2001) ]**PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed" target=new>PubMed Abstract

... A concentration of 47.6 mmol/L of citric acid (pH 2.3) in water led to total cell death within three minutes of incubation. Media containing 23.8 mmol/L and 47.6 mmol/L of citric acid exerted strong cytotoxicity (47 to 90 per cent of cell death) and inhibited protein synthesis (IC50 = 0.28 per cent) of GF within three hours of incubation. Incubation of cells in a medium containing 11.9 mmol/L of citric acid also suppressed the attachment and spreading of fibroblasts on culture plates and Type I collagen, with 58 per cent and 22 per cent of inhibition, respectively. Culture medium supplemented with 11.9, 23.8 and 47.6 mmol/L of citric acid also led to extracellular acidosis by decreasing the pH value from 7.5 to 6.3, 5.2 and 3.8, respectively. [Lan WC et al; Aust Dent J 44 (2): 123-30 (1999) ]**PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed" target=new>PubMed Abstract

INTERACTIONS:
... Citric acid aerosol inhalation caused decreases in dynamic respiratory compliance and forced expiratory volume in 0.1 s (FEV0.1). This airway constriction was significantly attenuated by MK-886, mepyramine, cromolyn sodium, and compound 48/80, but not by either methysergide or indomethacin. Both LTC4 and histamine infusion significantly increased the magnitude of citric acid-induced airway constriction in compound 48/80-pretreated guinea pigs. Citric acid inhalation caused significant increase in histamine level in the bronchoalveolar lavage sample, which

was significantly suppressed by compound 48/80. [Lin CH, Lai YL; Toxicol Appl Pharmacol 206 (3): 343-50 (2005) ]**PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed" target=new>PubMed Abstract

The relative efficacy of citric, malic, malonic, oxalic and succinic acids, and deferoxamine mesylate on the toxicity, distribution and excretion in mice exposed to aluminum were compared. Chelating agents were administered ip at a dose equal to one-fourth of their respective LD50. To determine the effect of the various chelators on the toxicity of aluminum, various doses of aluminum nitrate (938-3188 mg/kg) were administered ip, followed by one of the chelators. Survival was recorded at the end of 14 days. ... Malic acid and deferoxamine mesylate were the most effective in increasing the urinary excretion of aluminum. Citric acid was the most effective in increasing the fecal excretion of aluminum. Malonic, oxalic and succinic acids had no overall beneficial effects. Citric acid would appear to be the most effective agent of those tested in the prevention of acute aluminium intoxication. [Domingo JL et al; Hum Toxicol 7 (3): 259-62 (1988) ]**PEER REVIEWED**

... When aluminum hydroxide and citric acid (133 mg Al/kg and 62 mg/kg, respectively) were simultaneously given orally to mice, fetal skeletal development defects resulted. [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 2:373]**PEER REVIEWED**

The primary purpose of this study was to determine the relative usefulness of various measures to monitor body aluminum burden in weanling rats fed various amounts of aluminum (0.39 umol aluminum/g diet for 29 days, approximately 40 umol aluminum/g diet with or without citrate for 29 days and approximately 100 umol aluminum/g diet with citrate for 12 or 29 days) or injected ip with graded doses of aluminum (0.01, 4.6, 11.8, 23.5 or 94 umol aluminum). Twenty four hours prior to sacrifice, all rats were injected ip with either desferrioxamine (75 mg) or buffer. All seven indices of aluminum exposure monitored (eg: tibia, liver, kidney and serum aluminum concn; changes in serum aluminum concn in response to desferrioxamine; urinary aluminum excretion with and without desferrioxamine treatment) were highly ($p < 0.001$) correlated to parenteral aluminum exposure. Ingestion of citrate had small but significant effects on aluminum retention. /Citrate/ [Greger JL, Powers CF; Toxicol 76 (2): 119-32 (1992) ]**PEER REVIEWED**

A high dietary intake of citric acid was without effect on growth rate unless the animals were on a low-calcium diet, in which case a reduced body weight was observed. [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:767]**PEER REVIEWED**

Ingestion of citric acid may impair absorption of calcium and iron. [Sheftel, V.O.; Indirect Food Additives and Polymers. Migration and Toxicology. Lewis Publishers, Boca Raton, FL. 2000., p. 881]**PEER REVIEWED**

Citric acid increased the incidence of bladder carcinomas in F344 rats administered N-butyl-N-(4-hydroxybutyl)nitrosamine or N-ethyl-N-(4-hydroxybutyl)nitrosamine in drinking water, apparently due to a secondary effect of the acid, which increased water consumption and hence the dose of the test material. [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:768]**PEER REVIEWED**

PHARMACOLOGY:

THERAPEUTIC USES:

Mesh Heading: Anticoagulants, chelating Agents [National Library of Medicine, SIS; ChemIDplus Record for Citric acid (77-92-9). Available from, as of April 17, 2006: http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp]**PEER REVIEWED**

IT HAS ... BEEN USED TO DISSOLVE URINARY BLADDER CALCULI, & AS MILD ASTRINGENT. [Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975., p. 1260]**PEER REVIEWED**

Citrate ... of ... value in alleviation of chronic metabolic acidosis ... from chronic renal insufficiency or syndrome of renal tubular acidosis ... usually prescribed in form of sodium citrate and citric acid soln, USP ... [Goodman, L.S., and A. Gilman. (eds.) The Pharmacological Basis of Therapeutics. 5th ed. New York: Macmillan Publishing Co., Inc., 1975., p. 806]**PEER REVIEWED**

Component of anticoagulant citrate solutions (citrate dextrose soln; citrate phosphate dextrose soln; citric acid syrup). [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 406]**PEER REVIEWED**

Potassium citrate, up to 10 g daily, has been used as a potassium supplement; the potassium and sodium salts have been used, in similar dosages, as mild diuretics in humans. [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:768]**PEER REVIEWED**

DRUG WARNINGS:

A study of abdominal pain and severity of other side effects attributed to Picolax, a combination of citric acid, magnesium oxide and sodium picosulfate, was conducted among 267 patients, 55 of whom had inflammatory bowel disease, all of whom were given a full single dose of Picolax as preparation for radiology or endoscopy. The frequency of increased abdominal pain and severe side effects after Picolax administration was similar in the patients with inflammatory bowel disease and the patients with other colonic disorders. None of the patients with iron deficiency in whom investigations had yielded negative results reported severe side effects; this was significantly different from the proportion reporting severe side effects among the patients with inflammatory bowel disease, the irritable bowel syndrome and diverticular disease. The increase in the mean number of stools/24 hr after Picolax was lower in the patients with inflammatory bowel disease than in the other diagnostic groups. On review 2-4 wk after examination none of the patients with inflammatory bowel disease reported deterioration in their symptoms. [McDonagh AJ et al; Br Med J 299: 776-7 (1989) ]**PEER REVIEWED**

Following the occurrence of aluminum encephalopathy in four patients with chronic renal failure, 34 azotemic patients seen during the same year and five volunteers who took varying combinations of aluminum hydroxide and an alkalinizing citrate (Shohl's) solution were studied. It was found that the four encephalopathic cases were older than the 34 azotemic patients (68 years + or - 14 standard deviation, versus 50 + or - 13, $p < 0.05$), had a higher mean serum aluminum value (727 ug/l + or - 320 versus 92 + or - 73, $p < 0.005$), had taken more aluminum hydroxide (5 g/day + or - 0.9 versus 1.6 + or - 1.8, $p < 0.01$), and more Shohl's solution (64 ml/day + or - 19 versus 20 + or - 29, $p < 0.01$). In all 38 patients the serum aluminum values correlated directly with age ($p= 0.01$), aluminum hydroxide ($p= 0.001$) and concomitant citrate intake ($p= 0.004$). In the five healthy volunteers the 24 hr urinary aluminum excretion increased from a baseline of 22 ug + or - 19 standard deviation to 167 + or - 109 ($p= 0.05$) during aluminum hydroxide intake, rising to 580 + or - 267 ($p= 0.01$) during the simultaneous intake of citrate and aluminum hydroxide. Corresponding serum aluminum values were 11 ug/l + or - 2 standard deviation, 44 + or - 34 ($p= 0.1$), and 98 + or - 58 ($p < 0.05$). Thus citrate seems to enhance aluminum absorption and may cause encephalopathy in patients with chronic renal failure, especially the elderly.[Bakir AA et al; Clin Nephrol 31 (1): 40-4 (1989)]**PEER REVIEWED**

INTERACTIONS:

... Citric acid aerosol inhalation caused decreases in dynamic respiratory compliance and forced expiratory volume in 0.1 s (FEV0.1). This airway constriction was significantly attenuated by MK-886, mepyramine, cromolyn sodium, and compound 48/80, but not by either methysergide or indomethacin. Both LTC4 and histamine infusion significantly increased the magnitude of citric acid-induced airway constriction in compound 48/80-pretreated guinea pigs. Citric acid inhalation caused significant

increase in histamine level in the bronchoalveolar lavage sample, which was significantly suppressed by compound 48/80. [Lin CH, Lai YL; Toxicol Appl Pharmacol 206 (3): 343-50 (2005) ]**PEER REVIEWED** <a href="http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed" target=new>PubMed Abstract

The relative efficacy of citric, malic, malonic, oxalic and succinic acids, and deferoxamine mesylate on the toxicity, distribution and excretion in mice exposed to aluminum were compared. Chelating agents were administered ip at a dose equal to one-fourth of their respective LD50. To determine the effect of the various chelators on the toxicity of aluminum, various doses of aluminum nitrate (938-3188 mg/kg) were administered ip, followed by one of the chelators. Survival was recorded at the end of 14 days. ... Malic acid and deferoxamine mesylate were the most effective in increasing the urinary excretion of aluminum. Citric acid was the most effective in increasing the fecal excretion of aluminum. Malonic, oxalic and succinic acids had no overall beneficial effects. Citric acid would appear to be the most effective agent of those tested in the prevention of acute aluminium intoxication. [Domingo JL et al; Hum Toxicol 7 (3): 259-62 (1988) ]**PEER REVIEWED**

... When aluminum hydroxide and citric acid (133 mg Al/kg and 62 mg/kg, respectively) were simultaneously given orally to mice, fetal skeletal development defects resulted. [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 2:373]**PEER REVIEWED**

The primary purpose of this study was to determine the relative usefulness of various measures to monitor body aluminum burden in weanling rats fed various amounts of aluminum (0.39 umol aluminum/g diet for 29 days, approximately 40 umol aluminum/g diet with or without citrate for 29 days and approximately 100 umol aluminum/g diet with citrate for 12 or 29 days) or injected ip with graded doses of aluminum (0.01, 4.6, 11.8, 23.5 or 94 umol aluminum). Twenty four hours prior to sacrifice, all rats were injected ip with either desferrioxamine (75 mg) or buffer. All seven indices of aluminum exposure monitored (eg: tibia, liver, kidney and serum aluminum concn; changes in serum aluminum concn in response to desferrioxamine; urinary aluminum excretion with and without desferrioxamine treatment) were highly ($p < 0.001$) correlated to parenteral aluminum exposure. Ingestion of citrate had small but significant effects on aluminum retention. /Citrate/ [Greger JL, Powers CF; Toxicol 76 (2): 119-32 (1992) ]**PEER REVIEWED**

A high dietary intake of citric acid was without effect on growth rate unless the animals were on a low-calcium diet, in which case a reduced body weight was observed. [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:767]**PEER REVIEWED**

Ingestion of citric acid may impair absorption of calcium and iron. [Sheftel, V.O.; Indirect Food Additives and Polymers. Migration and Toxicology. Lewis Publishers, Boca Raton, FL. 2000., p. 881]**PEER REVIEWED**

Citric acid increased the incidence of bladder carcinomas in F344 rats administered N-butyl-N-(4-hydroxybutyl)nitrosamine or N-ethyl-N-(4-hydroxybutyl)nitrosamine in drinking water, apparently due to a secondary effect of the acid, which increased water consumption and hence the dose of the test material. [Bingham, E.; Cohrssen, B.; Powell, C.H.; Patty's Toxicology Volumes 1-9 5th ed. John Wiley & Sons. New York, N.Y. (2001)., p. 5:768]**PEER REVIEWED**

ENVIRONMENTAL FATE & EXPOSURE:

ENVIRONMENTAL FATE/EXPOSURE SUMMARY:

Citric acid's production and use as an acidulant in beverages, confectionery, effervescent salts, in pharmaceutical syrups, elixirs; in processing cheese, in chemical manufacture, a foam inhibitor, a sequestering agent, a mordant, in electroplating, in special inks, an anticoagulant, and in water-conditioning agent and detergent builder may result in its release to the environment through various waste streams. Citric acid is widely distributed in plants and in animal tissues and fluids. If released to air, an estimated vapor pressure of 1.66X10-8 mm Hg at 25 deg C indicates citric acid will exist solely in the particulate phase in the atmosphere. Particulate-phase citric acid will be removed from the atmosphere by wet or dry deposition. Citric acid does not contain chromophores that absorb at wavelengths > 290 nm and therefore is not expected to be susceptible to direct photolysis by sunlight. If released to soil, citric acid is expected to have very high mobility based upon an estimated Koc of 3.1. The pKa of citric acid is 2.79, indicating that this compound will primarily exist in the anion form in the environment and anions generally do not adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts. Volatilization from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry's Law constant of 4.3X10-14 atm-cu m/mole. Citric acid is not expected to volatilize from dry soil surfaces based upon its estimated vapor pressure. Citric acid may be susceptible to biodegradation in terrestrial environments based on the observed degradation of 53-100% in sludge inoculum after time periods ranging from 1 to 42 days. If released into water, citric acid is not expected to adsorb to suspended solids and sediment based upon the estimated Koc. Screening tests show that citric acid is readily biodegradable in aquatic environments reaching 66.4% and 67.3% of its theoretical BOD after 5 days using freshwater and seawater inoculums, respectively. Volatilization from water surfaces is

not expected to be an important fate process based upon this compound's estimated Henry's Law constant. An estimated BCF of 3.2 suggests the potential for bioconcentration in aquatic organisms is low. Hydrolysis is not expected to be an important environmental fate process since this compound lacks functional groups that hydrolyze under environmental conditions. Occupational exposure to citric acid may occur through dermal contact with this compound at workplaces where citric acid is produced or used. Monitoring data indicate that the general population may be exposed to citric acid via ingestion of food and dermal contact with this compound and other products containing citric acid. (SRC) **PEER REVIEWED**

PROBABLE ROUTES OF HUMAN EXPOSURE:

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,691,218 workers (1,083,005 of these are female) are potentially exposed to citric acid in the US(1). Occupational exposure to citric acid may occur through dermal contact with this compound at workplaces where citric acid is produced or used(SRC). Monitoring data indicate that the general population may be exposed to citric acid via ingestion of food and dermal contact with this compound and other products containing citric acid(SRC). [(1) NIOSH; International Safety Cards. Citric Acid. 77-92-9. Available at http//www.cdc.gov/niosh/ipcs/nicstart.html as of April 26, 2006. ]**PEER REVIEWED**

BODY BURDEN:

Citric acid was found to be excreted by humans through urine at a rate of 3-17 mg/kg body weight/day and through sweat at 0.2 mg/100 ml(1). [(1) Verschueren K; Handbook of Environmental Data on Organic Chemicals, Vol 1-2, 4th ed. John Wiley and Sons; New York, NY (2001) ]**PEER REVIEWED**

NATURAL POLLUTION SOURCES:

Citric acid is widely distributed in plants and in animal tissues and fluids(1). It is extremely widespread in nature and has been identified in flowers of Hibiscus subdariffa(2). [(1) O'Neil MJ, ed; The Merck Index. 13th ed. Whitehouse Station, NJ: Merck and Co., Inc. p. 405 (2001) (2) Furia TE, Bellanca N, eds; Fenaroli's Handbook of Flavor Ingredients. Volume 2. 2nd ed. Cleveland, OH: The Chemical Rubber Co. p. 78 (1975) ]**PEER REVIEWED**

ARTIFICIAL POLLUTION SOURCES:

Citric acid's production and use as an acidulant in beverages, confectionery, effervescent salts, in pharmaceutical syrups, elixirs, to adjust the pH of foods and as synergistic antioxidant, in processing cheese, in chemical manufacture, a foam inhibitor, a sequestering agent, a mordant, in electroplating, in special inks, an anticoagulant, and in water-conditioning agent and detergent builder(1,2) may result in its release to the environment through various waste streams(SRC). [(1) O'Neil MJ, ed; The Merck Index. 13th ed. Whitehouse Station, NJ: Merck and Co., Inc. p. 405 (2001) (2) Lewis RJ Sr, ed; Hawley's Condensed Chemical

Dictionary. 14th ed. NY, NY: John Wiley & Sons, p. 272 (2001) ]**PEER REVIEWED**

ENVIRONMENTAL FATE:

TERRESTRIAL FATE: Based on a classification scheme(1), an estimated Koc value of 3.1(SRC), determined from a log Kow of -1.64(2) and a regression-derived equation(3), indicates that citric acid is expected to have very high mobility in soil(SRC). The pKa of citric acid is 2.79(4), indicating that this compound will primarily exist in the anion form in the environment and anions generally do not adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts(5). Volatilization of citric acid from moist soil surfaces is not expected to be an important fate process(SRC) given an estimated Henry's Law constant of 4.3X10-14 atm-cu m/mole(SRC) derived from its estimated vapor pressure, 1.66X10-8 mm Hg(6), and water solubility, 3.83X10+5 mg/L(7). Citric acid is not expected to volatilize from dry soil surfaces(SRC) based upon its estimated vapor pressure(6). Citric acid may be susceptible to biodegradation in terrestrial environments based on the observed degradation of 53-100% in sludge inoculum after time periods ranging from 1 to 42 days(8-10). [(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Sirius Technical Application Notes. Vol 1. East Sussex, England: Sirius Analytical Instruments Ltd, ISBN 901125 00 9, p. 168 (1995) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 4-9 (1990) (4) Serjeant EP, Dempsey B; Ionisation constants of organic acids in aqueous solution. IUPAC Chem Data Ser No.23. NY,NY: Pergamon pp. 989 (1979) (5) Doucette WJ; pp. 141-188 in Handbook of Property Estimation Methods for Chemicals. Boethling RS, Mackay D, eds. Boca Raton, FL: Lewis Publ (2000) (6) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Supplement 1. New York, NY: Hemisphere Pub Corp (1991) (7) Yalkowsky SH, He Y, eds; Handbook of aqueous solubility data. Boca Raton, FL: CRC Press p. 278 (2003) (8) Gerike P, Fischer WK; Ecotox Environ Safety 3: 159-73 (1979) (9) Heukelekian H, Rand MC; J Water Pollut Contr Assoc 27: 1040-53 (1955) (10) Placak OR, Ruchhoft CC; Sewage Works J 19: 423-40 (1947) ]**PEER REVIEWED**

AQUATIC FATE: Based on a classification scheme(1), an estimated Koc value of 3.1(SRC), determined from a log Kow of -1.64(2) and a regression-derived equation(3), indicates that citric acid is not expected to adsorb to suspended solids and sediment(SRC). The pKa of citric acid is 2.79(4), indicating that this compound will primarily exist in the anion form in the environment and anions generally do not adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts(5). Volatilization from water surfaces is not expected(3) based upon an estimated Henry's Law constant of 4.3X10-14 atm-cu m/mole(SRC) derived from its estimated vapor pressure, 1.66X10-8 mm Hg(6), and water solubility, 3.83X10+5 mg/L(7). According to a classification scheme(8), an estimated BCF of 3.2(SRC), from its log Kow(2) and a

regression-derived equation(9), suggests the potential for bioconcentration in aquatic organisms is low(SRC). Screening tests show that citric acid is readily biodegradable in aquatic environments reaching 53-100% degradation in sludge inoculum(10-12) and 66.4% and 67.3% of its theoretical BOD after 5 days using freshwater and seawater inoculums, respectively(13). [(1) Swann RL et al; Res Rev 85: 17-28 (1983) (2) Sirius Technical Application Notes. Vol 1. East Sussex, England: Sirius Analytical Instruments Ltd, ISBN 901125 00 9, p. 168 (1995) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 4-9, 15-1 to 15-29 (1990) (4) Serjeant EP, Dempsey B; Ionisation constants of organic acids in aqueous solution. IUPAC Chem Data Ser No.23. NY,NY: Pergamon pp. 989 (1979) (5) Doucette WJ; pp. 141-188 in Handbook of Property Estimation Methods for Chemicals. Boethling RS, Mackay D, eds, Boca Raton, FL: Lewis Publ (2000) (6) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Supplement 1. New York, NY: Hemisphere Pub Corp (1991) (7) Yalkowsky SH, He Y, eds; Handbook of aqueous solubility data. Boca Raton, FL: CRC Press p. 278 (2003) (8) Franke C et al; Chemosphere 29: 1501-14 (1994) (9) Meylan WM et al; Environ Toxicol Chem 18: 664-72 (1999) (10) Gerike P, Fischer WK; Ecotox Environ Safety 3: 159-73 (1979) (11) Heukelekian H, Rand MC; J Water Pollut Contr Assoc 27: 1040-53 (1955) (12) Placak OR, Ruchhoft CC; Sewage Works J 19: 423-40 (1947) (13) Takemoto S et al; Suishitsu Odaku Kenkyu 4: 80-90 (1981) ]**PEER REVIEWED**

ATMOSPHERIC FATE: According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), citric acid, which has an estimated vapor pressure of 1.66X10-8 mm Hg at 25 deg C(2), is expected to exist solely in the particulate phase in the ambient atmosphere. Particulate-phase citric acid may be removed from the air by wet or dry deposition(SRC). Citric acid does not contain chromophores that absorb at wavelengths > 290 nm and therefore is not expected to be susceptible to direct photolysis by sunlight(3). [(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Supplement 1. New York, NY: Hemisphere Pub Corp (1991) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 7-4, 7-5, 8-12 (1990) ]**PEER REVIEWED**

ENVIRONMENTAL BIODEGRADATION:

AEROBIC: The biodegradability of citric acid was determined in six different tests and results found it to be well degraded in all tests(1). Citric acid achieved 93% DOC removal in a coupled units test (sludge inoculum), 85% DOC removal after 1 day in a Zahn-Wellens test (sludge inoculum), 100% DOC removal in an AFNOR test (42 days, germs inoculum simulating polluted river water), 100% DOC removal in a Sturm test (42 days, sewage treatment plant effluent), 100% DOC removal in an OECD screening test (19 days, effluent simulating surface water), and 90% BODT in a closed bottle test (30 days, effluent simulating surface water)(1).

Citric acid reached 53% of its theoretical BOD in 5 days using a sludge inoculum(2). Citric acid, present at 500 mg/L, reached 46% of its theoretical oxygen demand in 12 hours using a phenol acclimated activated sludge inoculum(3). In NASA wastewater inoculated with batch microbial cultures, citric acid (5 mg/ml) was degraded more than 50% after 15 days by Achromobacter sp.(4). Citric acid, present at 500 mg/L, reached 98.4% of its theoretical BOD in 22 to 24 hours using an activated sludge inoculum at 2,228 mg/L(5). Citric acid (1% w/v) displayed BOD values of 6,410 and 6,040 mg/L using a defined microbial mixture and sewage inoculums, respectively(6). Citric acid, present at 10 mg/L, reached 66.4% and 67.3% of its theoretical BOD after 5 days using freshwater and seawater inoculums, respectively(7). [(1) Gerike P, Fischer WK; Ecotox Environ Safety 3: 159-73 (1979) (2) Heukelekian H, Rand MC; J Water Pollut Contr Assoc 27: 1040-53 (1955) (3) McKinney RE et al; Sew Indust Wastes 28: 547-57 (1956) (4) Nwankwoala AU et al; Biodegradation 10: 105-12 (1999) (5) Placak OR, Ruchhoft CC; Sewage Works J 19: 423-40 (1947) (6) Sharma A et al; Bull Environ Contam Toxicol 57: 34-40 (1996) (7) Takemoto S et al; Suishitsu Odaku Kenkyu 4: 80-90 (1981) ]**PEER REVIEWED**

ENVIRONMENTAL ABIOTIC DEGRADATION:

The rate constant for the vapor-phase reaction of citric acid with photochemically-produced hydroxyl radicals has been estimated as 7.0X10-12 cu cm/molecule-sec at 25 deg C(SRC) using a structure estimation method(1). This corresponds to an atmospheric half-life of about 55 hours at an atmospheric concentration of 5X10+5 hydroxyl radicals per cu cm(1). A citric acid aqueous solution (pH 1), with a hydroxy radical concentration of 1X10-17 mol/L, had a reaction rate constant of 3.0X10+7 L/mol-sec at room temperature(2). This corresponds to a calculated half-life of 73 years(2). Citric acid is not expected to undergo hydrolysis in the environment due to the lack of functional groups that hydrolyze under environmental conditions(3). Citric acid does not contain chromophores that absorb at wavelengths > 290 nm and therefore is not expected to be susceptible to direct photolysis by sunlight(1). [(1) Meylan WM, Howard PH; Chemosphere 26: 2293-99 (1993) (2) Anbar M, Neta P; Int J of Appl Radiation and Isotopes 18:493-523 (1967) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 7-4, 7-5, 8-12 (1990) ]**PEER REVIEWED**

ENVIRONMENTAL BIOCONCENTRATION:

An estimated BCF of 3.2 was calculated for citric acid(SRC), using a log Kow of -1.64(1) and a regression-derived equation(2). According to a classification scheme(3), this BCF suggests the potential for bioconcentration in aquatic organisms is low(SRC). [(1) Sirius Technical Application Notes. Vol 1. East Sussex, England: Sirius Analytical Instruments Ltd, ISBN 901125 00 9, p. 168 (1995) (2) Meylan WM et al; Environ Toxicol Chem 18: 664-72 (1999) (3) Franke C et al; Chemosphere 29: 1501-14 (1994) ]**PEER REVIEWED**

SOIL ADSORPTION/MOBILITY:

The Koc of citric acid is estimated as 3.1(SRC), using a log Kow of -1.64(1) and a regression-derived equation(2). According to a classification scheme(3), this estimated Koc value suggests that citric acid is expected to have very high mobility in soil. The pKa of citric acid is 2.79(4), indicating that this compound will primarily exist as the anion in the environment and anions generally do not adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts(5). A 2 uM solution of citric acid in Gulfstream seawater showed equilibrium absorption values of 79% and 94% onto 0.01 and 0.25 g of hydroxyapatite, respectively(6). [(1) Sirius Technical Application Notes. Vol 1. East Sussex, England: Sirius Analytical Instruments Ltd, ISBN 901125 00 9, p. 168 (1995) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 4-9 (1990) (3) Swann RL et al; Res Rev 85: 17-28 (1983) (4) Serjeant EP, Dempsey B; Ionisation constants of organic acids in aqueous solution. IUPAC Chem Data Ser No.23. NY,NY: Pergamon pp. 989 (1979) (5) Doucette WJ; pp. 141-188 in Handbook of Property Estimation Methods for Chemicals. Boethling RS, Mackay D, eds. Boca Raton, FL: Lewis Publ (2000) (6) Gordon AS, Millero FJ; Microb Ecol 11: 289-98 (1985) ]**PEER REVIEWED**

VOLATILIZATION FROM WATER/SOIL:

The Henry's Law constant for citric acid is estimated as 4.3X10-14 atm-cu m/mole(SRC) derived from its estimated vapor pressure, 1.66X10-8 mm Hg(1), and water solubility, 3.83X10+5 mg/L(2). This Henry's Law constant indicates that citric acid is expected to be essentially nonvolatile from water surfaces(3). Citric acid's estimated Henry's Law constant indicates that volatilization from moist soil surfaces is not expected to occur(SRC). Citric acid is not expected to volatilize from dry soil surfaces(SRC) based upon its estimated vapor pressure(1). [(1) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Supplement 1. New York, NY: Hemisphere Pub Corp (1991) (2) Yalkowsky SH, He Y, eds; Handbook of aqueous solubility data. Boca Raton, FL: CRC Press p. 278 (2003) (3) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) ]**PEER REVIEWED**

FOOD SURVEY VALUES:

MID, TO INCR EFFECTIVENESS OF ANTIOXIDANTS IN LARD, SHORTENING, & UNSMOKED DRY SAUSAGE; @ 0.01% ALONE OR WITH ANTIOXIDANTS IN LARD OR SHORTENING; 0.001% IN ... SAUSAGE WITH 0.003% BHA. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 823]**PEER REVIEWED**

Citric acid was detected as a flavoring constituent of farine collected from St. Lucia in the Caribbean(1). [(1) Dougan J et al; J Sci Food Agric 34:874-84 (1983) ]**PEER REVIEWED**

ENVIRONMENTAL STANDARDS & REGULATIONS:

FIFRA REQUIREMENTS:

Tolerance exemptions for minimal risk active and inert ingredients. Unless specifically excluded, residues resulting from the use of the following substances as either an inert or an active ingredient in a pesticide chemical formulation, including antimicrobial pesticide chemicals, are exempted from the requirement of a tolerance under FFDCA section 408, if such use is in accordance with good agricultural or manufacturing practices. Citric acid is included on this list. [40 CFR 180.950; U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of June 21, 2006: http://www.gpoaccess.gov/ecfr]**PEER REVIEWED**

Section 4(g)(2)(A) of FIFRA requires the Agency to determine, after consideration of relevant data concerning an active ingredient whether products containing the active ingredient are eligible for reregistration. For products containing citric acid as an active ingredient the Agency has waived all generic data requirements except for those basic product identity and chemistry. These data were submitted and reviewed. In addition to these data, the Agency has considered the factors ... regarding citric acid's natural occurrence, common use as a food item, and the lack of reported adverse effects information. The Agency has completed its consideration of these data and other factors and has determined this information is sufficient to support reregistration of products containing citric acid as an active ingredient. [USEPA/Office of Pesticide Programs; Reregistration Eligibility Decision Document - Citric Acid (June 1992). Available from, as of June 21, 2006: http://cfpub.epa.gov/oppref/rereg/status.cfm?show=rereg]**PEER REVIEWED**

As the federal pesticide law FIFRA directs, EPA is conducting a comprehensive review of older pesticides to consider their health and environmental effects and make decisions about their future use. Under this pesticide reregistration program, EPA examines health and safety data for pesticide active ingredients initially registered before November 1, 1984, and determines whether they are eligible for reregistration. In addition, all pesticides must meet the new safety standard of the Food Quality Protection Act of 1996. Pesticides for which EPA had not issued Registration Standards prior to the effective date of FIFRA '88 were divided into three lists based upon their potential for human exposure and other factors, with List B containing pesticides of greater concern and List D pesticides of less concern. Citric acid is found on List D. Case No: 021801; Pesticide type: fungicide/ antimicobial; Case Status: RED Approved 08/92 - OPP has made a decision that some/all uses of the pesticide are eligible for reregistration, as reflected in a Reregistration Eligibility Decision (RED) Document.; Active ingredient

(AI): Citric acid; AI Status: RED Completed - OPP has completed a Reregistration Eligibility Decision (RED) document for the case/AI. [United States Environmental Protection Agency/ Prevention, Pesticides and Toxic Substances; Status of Pesticides in Registration, Reregistration, and Special Review. (1998) EPA 738-R-98-002, p. 302]**PEER REVIEWED**

FDA REQUIREMENTS:

Substance added directly to human food affirmed as generally recognized as safe (GRAS). [21 CFR 184.1033; U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of June 21, 2006: http://www.gpoaccess.gov/ecfr]**PEER REVIEWED**

Citric acid used as a general purpose food additive in animal drugs, feeds, and related products is generally recognized as safe when used in accordance with good manufacturing or feeding practice. [21 CFR 582.1033; U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of June 21, 2006: http://www.gpoaccess.gov/ecfr]**PEER REVIEWED**

Citric acid used as a sequestrant in animal drugs, feeds, and related products is generally recognized as safe when used in accordance with good manufacturing or feeding practice. [21 CFR 582.6033; U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of June 21, 2006: http://www.gpoaccess.gov/ecfr]**PEER REVIEWED**

Drug products containing certain active ingredients offered over-the-counter (OTC) for certain uses. A number of active ingredients have been present in OTC drug products for various uses, as described below. However, based on evidence currently available, there are inadequate data to establish general recognition of the safety and effectiveness of these ingredients for the specified uses: citric acid is included in weight control drug products. [21 CFR 310.545; U.S. National Archives and Records Administration's Electronic Code of Federal Regulations. Available from, as of June 21, 2006: http://www.gpoaccess.gov/ecfr]**PEER REVIEWED**

ALLOWABLE TOLERANCES:

Residues of citric acid are exempted from the requirement of a tolerance when used as a sequestrant in accordance with good agricultural practices as inert (or occasionally active) ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest. [40 CFR 180.1001(c) (7/1/91)]**PEER REVIEWED**

Citric acid is exempted from the requirement of a tolerance when used as a buffer in accordance with good agricultural practice as inert (or occasionally active) ingredients in pesticide formulations applied to

animals. [40 CFR 180.1001(e) (7/1/91)]**PEER REVIEWED**

CHEMICAL/PHYSICAL PROPERTIES:

MOLECULAR FORMULA:
C6-H8-O7 [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 405]**PEER REVIEWED**

MOLECULAR WEIGHT:
192.12 [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 405]**PEER REVIEWED**

COLOR/FORM:
Crystals; monoclinic holohedra; crystallizes from hot concentrated aqueous solution [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 405]**PEER REVIEWED**

Colorless, translucent crystals or powder [Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 14th Edition. John Wiley & Sons, Inc. New York, NY 2001., p. 272]**PEER REVIEWED**

Rhombic crystals from water with 1 mol of water of crystallization [Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 73rd ed. Boca Raton, FL: CRC Press Inc., 1992-1993., p. 3-183]**PEER REVIEWED**

ODOR:
Odorless [Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 14th Edition. John Wiley & Sons, Inc. New York, NY 2001., p. 272]**PEER REVIEWED**

TASTE:
Strongly acid taste [Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 14th Edition. John Wiley & Sons, Inc. New York, NY 2001., p. 272]**PEER REVIEWED**

Pleasant, sweet, tart taste [Lopez-Garcia R; Kirk-Othmer Encyclopedia of Chemical Technology. (2005). NY, NY: John Wiley & Sons; Citric Acid. Online Posting Date: April 19, 2002. ]**PEER REVIEWED**

BOILING POINT:
Decomposes [Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 14th Edition. John Wiley & Sons, Inc. New York, NY 2001., p. 272]**PEER REVIEWED**

MELTING POINT:
153 deg C [Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 14th Edition. John Wiley & Sons, Inc. New York, NY 2001., p. 272]**PEER REVIEWED**

CORROSIVITY:
WILL CORRODE COPPER, ZINC, ALUMINUM AND THEIR ALLOYS [U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5., p. ]**PEER REVIEWED**

DENSITY/SPECIFIC GRAVITY:
1.665 g/cu cm at 20 deg C [Lide, D.R. CRC Handbook of Chemistry and Physics 86TH Edition 2005-2006. CRC Press, Taylor & Francis, Boca Raton, FL 2005, p. 3-120]**PEER REVIEWED**

DISSOCIATION CONSTANTS:
pKa = 2.79 [Serjeant, E.P., Dempsey B.; Ionisation Constants of Organic Acids in Aqueous Solution. International Union of Pure and Applied Chemistry (IUPAC). IUPAC Chemical Data Series No. 23, 1979. New York, New York: Pergamon Press, Inc., p. 989]**PEER REVIEWED**

HEAT OF COMBUSTION:
-474.5 KCAL/MOLE [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 244]**PEER REVIEWED**

OCTANOL/WATER PARTITION COEFFICIENT:
log Kow = -1.64 [Sirius Technical Application Notes. Vol 1. East Sussex, England: Sirius Analytical Instruments Ltd, ISBN 901125 00 9, p. 168 (1995) ]**PEER REVIEWED**

SOLUBILITIES:
Solubility in water: 54.0% w/w at 10 deg C; 59.2% at 20 deg C; 64.3% at 30 deg C; 68.6% at 40 deg C; 70.9% at 50 deg C; 73.5% at 60 deg C; 76.2% at 70 deg C; 78.8% at 80 deg C; 81.4% at 90 deg C; 84.0% at 100 deg C [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 405]**PEER REVIEWED**

Very soluble in ethanol; soluble in ether, ethyl acetate; insoluble in benzene, chloroform [Lide, D.R. CRC Handbook of Chemistry and Physics 86TH Edition 2005-2006. CRC Press, Taylor & Francis, Boca Raton, FL 2005, p. 3-120]**PEER REVIEWED**

In water solubility, 3.83X10+5 mg/L at 25 deg C [Yalkowsky, S.H., He, Yan., Handbook of Aqueous Solubility Data: An Extensive Compilation of Aqueous Solubility Data for Organic Compounds Extracted from the AQUASOL

dATAbASE. CRC Press LLC, Boca Raton, FL. 2003., p. 278]**PEER REVIEWED**

SPECTRAL PROPERTIES:

SADTLER REFERENCE NUMBER: 765 (IR, PRISM) [Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979., p. C-251]**PEER REVIEWED**

IR: 5104 (Coblentz Society Spectral Collection) [Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V5: 4381]**PEER REVIEWED**

1H NMR: 7552 (Sadtler Research Laboratories Spectral Collection) [Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V5: 4381]**PEER REVIEWED**

MASS: 8394 (NIST/EPA/MSDC Mass Spectral Database 1990 version) [Lide, D.R., G.W.A. Milne (eds.). Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. 1994., p. V5: 4381]**PEER REVIEWED**

VAPOR PRESSURE:

1.7X10-8 mm Hg at 25 deg C (est) [Daubert, T.E., R.P. Danner. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, D.C.: Taylor and Francis, 1989., p. ]**PEER REVIEWED**

VISCOSITY:

6.5 cP 50% aqueous solution at 25 deg C [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 244]**PEER REVIEWED**

OTHER CHEMICAL/PHYSICAL PROPERTIES:

Orthorhombic crystals from cold aqueous solutions; pleasant, sour taste; density = 1.542; melting point at about 100 deg C; loses water of crystallization in dry air or when heated at about 40 to 50 deg C; slightly deliquescent in moist air; softens at 75 deg C; pH of 0.1 N solution = 2.2; densities of aqueous solution (15 deg C/15 deg C): 10% = 1.0392, 20% = 1.0805, 30% = 1.1244, 40% = 1.1709, 50% = 1.2204, 60% = 1.2738 /Citric Acid Monohydrate/ [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 405]**PEER REVIEWED**

A:B:C= 0.674:1:1.662; CRYSTALS BRACHYDOMATIC WITH (011), (110), (101), (111) ETC, PERFECT 001 CLEAVAGE /CITRIC ACID MONOHYDRATE/ [The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976., p. 300]**PEER REVIEWED**

HEAT OF COMBUSTION: -471.4 KCAL/MOLE /CITRIC ACID MONOHYDRATE/ [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 244]**PEER REVIEWED**

Heat of formation = -1548.8 kJ/mol at 25 deg C [Lide, D.R. CRC Handbook of Chemistry and Physics 86TH Edition 2005-2006. CRC Press, Taylor & Francis, Boca Raton, FL 2005, p. 5-31]**PEER REVIEWED**

Solubility in g/100 g saturated solution: ether 2.17; chloroform 0.007; amyl alcohol 15.43; amyl acetate 5.98; ethyl acetate 5.28 /Citric Acid Monohydrate [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 405]**PEER REVIEWED**

Solubility at 19 deg C in g/100 g solvent: methanol 197; propanol 62.8 /Citric Acid Monohydrate/ [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 405]**PEER REVIEWED**

INDEX OF REFRACTION: 1.493, 1.498, 1.509 @ 20 DEG C /CITRIC ACID HYDRATE/ [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 244]**PEER REVIEWED**

DENSITY: 1.542 @ 18 DEG C/4 DEG C /CITRIC ACID HYDRATE/ [Weast, R.C. (ed.). Handbook of Chemistry and Physics. 60th ed. Boca Raton, Florida: CRC Press Inc., 1979., p. C-251]**PEER REVIEWED**

BULK DENSITY: 56.2 LB/CU FT; HEAT OF SOLN: -3.9 KCAL/MOLE; BUFFERING INDEX: 2.46; STD FREE ENERGY OF ANION FORMATION: -278.8 KCAL FOR AQ SOLN @ 25 DEG C [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 244]**PEER REVIEWED**

Hydrated form is efflorescent in dry air /Citric acid Hydrate/ [Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 14th Edition. John Wiley & Sons, Inc. New York, NY 2001., p. 272]**PEER REVIEWED**

Henry's Law constant = 4.3X10-14 atm-cu m/mol at 25 deg C (est) [SRC; The Physical Properties Database (PHYSPROP). Syracuse, NY: Syracuse Res Corp. Available from, as of April 26, 2006: http://www.syrres.com/esc/physprop.htm]**PEER REVIEWED**

Hydroxyl radical reaction rate constant = 7.0X10-12 cu cm/molec-sec at 25 deg C (est) [US EPA; Estimation Program Interface (EPI) Suite. Ver.3.12. Nov 30, 2004. Available from, as of Apr 26, 2006: http://www.epa.gov/oppt/exposure/docs/episuitedl.htm]**PEER REVIEWED**

CHEMICAL SAFETY & HANDLING:

SKIN, EYE AND RESPIRATORY IRRITATIONS:
Inhalation of dust irritates nose and throat. Contact with eyes causes irritation. [U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5., p. ]**PEER REVIEWED**

FIRE POTENTIAL:
Combustible liquid [Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 955]**PEER REVIEWED**

FLAMMABLE LIMITS:
0.28-2.29 KG/CU M (DUST) [U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5., p. ]**PEER REVIEWED**

AUTOIGNITION TEMPERATURE:
1850 DEG F (POWDER) [U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5., p. ]**PEER REVIEWED**

FIRE FIGHTING PROCEDURES:
/EXTINGUISH WITH/ WATER, FOAM, DRY CHEM, CARBON DIOXIDE. [U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5., p. ]**PEER REVIEWED**

EXPLOSIVE LIMITS & POTENTIAL:
During vacuum evaporation of an aqueous mixture of unspecified mixed metal nitrates and citric acid, the amorphous solid exploded when nearly dry. This was attributed to oxidation of the organic residue by the nitrates present, possibly catalyzed by one of the oxides expected to be produced. /Metal nitrates/ [Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990, p. 1672]**PEER REVIEWED**

HAZARDOUS REACTIVITIES & INCOMPATIBILITIES:
Pharmaceutical incompatibilities: Potassium tartrate, alkali, and alkaline earth carbonates and bicarbonates, acetates, sulfides. [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 406]**PEER REVIEWED**

Potentially explosive reaction with metal nitrates. [Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition.

Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 955]**PEER REVIEWED**

HAZARDOUS DECOMPOSITION:
When heated to decomposition it emits acrid smoke and fumes. [Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 955]**PEER REVIEWED**

BEHAVIOR IN FIRE: MELTS AND DECOMPOSES. THE REACTION IS NOT HAZARDOUS. [U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5., p. ]**PEER REVIEWED**

PROTECTIVE EQUIPMENT & CLOTHING:
DUST MASK; GOGGLES OR FACE SHIELD; PROTECTIVE GLOVES [U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5., p. ]**PEER REVIEWED**

PREVENTIVE MEASURES:
SRP: The scientific literature for the use of contact lenses in industry is conflicting. The benefit or detrimental effects of wearing contact lenses depend not only upon the substance, but also on factors including the form of the substance, characteristics and duration of the exposure, the uses of other eye protection equipment, and the hygiene of the lenses. However, there may be individual substances whose irritating or corrosive properties are such that the wearing of contact lenses would be harmful to the eye. In those specific cases, contact lenses should not be worn. In any event, the usual eye protection equipment should be worn even when contact lenses are in place. **PEER REVIEWED**

STABILITY/SHELF LIFE:
Dilute aq solns may ferment on standing. [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 406]**PEER REVIEWED**

STORAGE CONDITIONS:
Crystalline citric acid, anhydrous, can be stored in dry form without difficulty, although conditions of high humidity and elevated temperatures should be avoided to prevent caking. Storage should be in tight containers to prevent exposure to moist air. Several granulations are commercially available with the larger particle sizes having less tendency toward caking. [Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V6 364 (1993)]**PEER REVIEWED**

Temperature: ambient; Venting: open. [U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5., p. ]**PEER REVIEWED**

Containers: 230 lb Barrels, bags, kegs, boxes, cartons, fiber drums, bottles. [Sax, N.I. Dangerous Properties of Industrial Materials Reports. New York: Van Nostrand Rheinhold, 1987., p. 9:4 (1989)]**PEER REVIEWED**

Separated from strong oxidants, strong bases, metal nitrates and metals. [IPCS, CEC; International Chemical Safety Card on Citric acid. (March 1998). Available from, as of April 19, 2006: http://www.inchem.org/documents/icsc/icsc/eics0855.htm]**PEER REVIEWED**

CLEANUP METHODS:

Addition of lime will neutralize and precipitate calcium citrate. [Sax, N.I. Dangerous Properties of Industrial Materials Reports. New York: Van Nostrand Rheinhold, 1987., p. 9:4 (1989)]**PEER REVIEWED**

DISPOSAL METHODS:

SRP: The most favorable course of action is to use an alternative chemical product with less inherent propensity for occupational exposure or environmental contamination. Recycle any unused portion of the material for its approved use or return it to the manufacturer or supplier. Ultimate disposal of the chemical must consider: the material's impact on air quality; potential migration in soil or water; effects on animal, aquatic, and plant life; and conformance with environmental and public health regulations. **PEER REVIEWED**

Inject at base of incinerator equipped with afterburner. Flammable solvent may be added. [Sax, N.I. Dangerous Properties of Industrial Materials Reports. New York: Van Nostrand Rheinhold, 1987., p. 9:4 (1989)]**PEER REVIEWED**

OCCUPATIONAL EXPOSURE STANDARDS:

MANUFACTURING/USE INFORMATION:

MAJOR USES:

For Citric acid (USEPA/OPP Pesticide Code: 21801) ACTIVE products with label matches. /SRP: Registered for use in the U.S. but approved pesticide uses may change periodically and so federal, state and local authorities must be consulted for currently approved uses./ [National Pesticide Informaton Retrieval System's USEPA/OPP Chemical Ingredients Database on Citric acid (77-92-9). Available from, as of April 20, 2006:

http://ppis.ceris.purdue.edu/htbin/epachem.com]**PEER REVIEWED**

Acidulant in beverages, confectionary, effervescent salts, in pharmaceutical syrups, elixirs, in effervescent powders and tablets, to adjust pH of foods and as a synergistic antioxidant in processing cheese. Used in beverages, jellies, jams, preserves and candy to provide tartness. In the manufacture of alkyd resins; in esterified form as plasticizer, foam inhibitor. In the manufacture of citric acid salts. As a sequestering agent to remove trace metals. As mordant to brighten colors; in special inks; in electroplating; in analytical chemistry for determinig citrate-soluble P2O5; as reagent for albumin, mucin, glucose, bile pigments. [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 405]**PEER REVIEWED**

Citric acid is utilized in a large variety of food and industrial applications because of its unique combination of properties. It is used as a acid to adjust pH, a buffer to control or maintain pH, a chelator to form stable complexes with multivalent metal ions, and a dispersing agent to stabilize emulsions and other multiphase systems. In addition, it has a pleasant, clean, tart taste making it useful in food and beverage products. [Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V6 368 (1993)]**PEER REVIEWED**

MEDICATION **PEER REVIEWED**

Flavoring extracts, confections, soft drinks, effervescent salts, acidifier, dispersing agent, medicines, water-conditioning agent & detergent builder, cleaning and polishing stainless steel and other metals, removal of sulfur dioxide from smelter waste gases, abscission of citrus fruit in harvesting, cultured dairy products [Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 14th Edition. John Wiley & Sons, Inc. New York, NY 2001., p. 272]**PEER REVIEWED**

To flavor oleomargarine and chili con carne; to accelerate color fixing in cured pork and beef cuts and in cured, comminuted meat food products. May be used in cured products to replace up to 50% of ascorbic acid, erythorbic acid, sodium ascorbate, or sodium erythorbate used. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 823]**PEER REVIEWED**

To prevent clotting of fresh beef blood, at 0.2%, with or without water; not more than 2 parts water to 1 part citric acid shall be used; to incr effectiveness of antioxidants in frozen, fresh pork sausage and freeze-dried meats, at 0.01% in combination with antioxidants. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 823]**PEER REVIEWED**

Excellent acidulant for hams, sausage, and soybean curds ... obtained by coating acid with ... animal or plant oils ... canned vegetables (other than those specifically regulated) may contain citric acid as acidulant ... optional ingredient in canning of prune juice and figs. ... Prevent off-flavors in fried potatoes. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 242]**PEER REVIEWED**

It is permitted in creamed cottage cheese, pasteurized process cheese, pasteurized cheese spreads and foods and cold pack cheese ... used ... as flavoring agent and to lower pH of dry cured cottage cheese. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 243]**PEER REVIEWED**

More flavorful buttermilk ... obtained when citric acid ... added to culture. Amount of volatile acids ... greatly incr when 0.2% citric acid ... incorporated in butter cultures. ... Treating milk for infant feeding with citric acid renders it more digestible by ... forming softer curd. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 243]**PEER REVIEWED**

Citric acid can be used for removing radioactive strontium from milk during fallout emergency. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 243]**PEER REVIEWED**

... Extensively employed in prepn of carbonated beverages to bring out flavor. ... Acts as preservative ... in syrup and finished product stage. ... Aids in imparting desired bouquet. ... inactivates trace metals which may cause haze or deterioration of color and flavor. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 243]**PEER REVIEWED**

... Employed in freeze-drying of fruit juices, in preserving bananas, and in drying raisins ... in wine ... adjust acidity, prevent cloudy ppt, and inhibit oxidation ... . Used to control pH for optimum gel formation ... adjust acidity of relishes, sauces, and other food products requiring ... flavor enhancement.  [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 243]**PEER REVIEWED**

... Incorporated in ... candy ... to enhance flavor of fruit, berries, and other ingredients, to prevent crystallization of sugar, to invert sucrose and to prevent oxidation of ingredients like nuts. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 244]**PEER REVIEWED**

... In enzyme prepn for clarifying fruit juices, in dry dough, baked farinaceous and crusty bakery products, and in antioxidants for chocolate and cocoa. ... Stabilizing agent for spices and onion powder. ... Synthesis of rearranged fats for shortening. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 245]**PEER REVIEWED**

... Production of foods from seaweed, prevention of discoloration of onions ... use with antioxidants in wrapping materials. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 245]**PEER REVIEWED**

... A synergist for antioxidants employed in inhibiting rancidity in foods containing fats and oils and in preventing loss of color and flavor of canned fruits and fish. A mixture of citric acids is used as a dip for oily fish to prevent surface tissue from becoming brown and gummy. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 244]**PEER REVIEWED**

MANUFACTURERS:

A.E. Staley Manufacturing Co., 2200 East Eldorado Street, P.O. Box 151, Decatur, IL 62525, (217) 423-4411; Tate & Lyle Citric Acid, 5600 Brentlinger Drive, Dayton, OH 45414; Production site: Dayton, OH 45414 [SRI Consulting. 2005 Directory of Chemical Producers - United States, Menlo Park, CA. 2005, p. 526]**PEER REVIEWED**

Archer Daniels Midland Co., 4666 Faries Parkway, Decatur, IL 62526, (217) 424-5200; ADM Corn Processing Division, P.O. Box 1470, Decatur, IL 62525; Production site: Southport, NC 28461 [SRI Consulting. 2005 Directory of Chemical Producers - United States, Menlo Park, CA. 2005, p. 526]**PEER REVIEWED**

Cargill Inc., P.O. Box 9300, Minneapolis, MN 55440, (952) 742-7575; Cargill Worldwide Acidulants, 400 East Diehl Rd., Suite 300, Naperville, IL 60563; Production site: Eddyville, IA 52553-5000 [SRI Consulting. 2005 Directory of Chemical Producers - United States, Menlo Park, CA. 2005, p. 526]**PEER REVIEWED**

METHODS OF MANUFACTURING:

The microbial production of citric acid on a commercial scale was begun in 1923 utilizing certain strains of Aspergillus niger to produce citric acid on the surface of a sucrose and salt solution. This tray fermentation technique is still used today, although it is being replaced by a submerged process known as deep tank fermentation. In the deep tank submerged process, Aspergillus niger mold spores are grown under controlled aseptic conditions on a test-tube slant and transferred to a seed tank or inoculum which is added to a fermentor along with pasteurized syrup. The pH is adjusted and nutrients added. Sterile air is sparged into

the fermentor while the sugar is converted to citric acid. The complete fermentation cycle can take as long as 15 days. ... Citric acid fermentation broth is generally separated from the biomass using filtration or centrifugation. The citric acid is usually purified using either a lime-sulfuric acid method or a liquid extraction process. [Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V6: 362 (1993)]**PEER REVIEWED**

Mold fermentation of beet or sugar cane molasses, or dextrose (corn sugar) **PEER REVIEWED**

Produced by mycological fermentation on an industrial scale using crude sugar solutions, such as molasses and strains of Aspergillus niger: ... Schweiger, US patent 2970084 (1961 to Miles Labs.) [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 405]**PEER REVIEWED**

...Extracted from citrus fruits (lemon juice contains 5 to 8%) and from pineapple waste. [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 405]**PEER REVIEWED**

By mold fermentation of carbohydrates, including deep fermentation, from lemon, lime, and pineapple juice, and from molasses. [Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 14th Edition. John Wiley & Sons, Inc. New York, NY 2001., p. 272]**PEER REVIEWED**

GENERAL MANUFACTURING INFORMATION:

... Dilute aqueous solutions are subject to molding (fermentation), oxalic acid being one of the fermentation products. [Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975., p. 1260]**PEER REVIEWED**

Applications: non-alcoholic beverages 2500 ppm; ice cream, ices, etc 1600 ppm; candy 4300 ppm; baked goods 1200 ppm; chewing gum 3600 ppm. [Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975., p. 101]**PEER REVIEWED**

To increase effectiveness of antioxidants in lard, shortening, & unsmoked dry sausage; at 0.01% alone or with antioxidants in lard or shortening; 0.001% in ... Sausage with 0.003% BHA. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 823]**PEER REVIEWED**

Citric acid solution one gal standard citric acid solution ... prepared by

placing 4 lb acid citric in gal measure & filling with hot water; mixture is agitated to dissolve acid. [Merory, J. Food Flavorings: Composition, Manufacture, and Use. 2nd ed. Westport, Conn.: Avi Publishing Co., 1968., p. 313]**PEER REVIEWED**

The chemical synthesis of citric acid was reported in 1880. Since then, many different synthetic routes have been investigated, reported, and patented. However, none of these have proven to be commercially feasible. [Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V6 364 (1993)]**PEER REVIEWED**

APPLICATIONS: NON-ALCOHOLIC BEVERAGES 2500 PPM; ICE CREAM, ICES, ETC 1600 PPM; CANDY 4300 PPM; BAKED GOODS 1200 PPM; CHEWING GUM 3600 PPM. [Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975., p. 101]**PEER REVIEWED**

FORMULATIONS/PREPARATIONS:

... Anticoagulant citrate dextrose solution, anticoagulant citrate phosphate dextrose solution, citric acid syrup, & effervescent salts. [Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975., p. 1260]**PEER REVIEWED**

Grades of purity: USP; reagent; monohydrate grade. [U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5., p. ]**PEER REVIEWED**

Grades: Both hydrous (hydrated) and anhydrous, Technical, Chemically Pure, United States Pharmacopeia, Food Chemical Codex. [Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 14th Edition. John Wiley & Sons, Inc. New York, NY 2001., p. 272]**PEER REVIEWED**

Citric acid for pharmaceutical use: not < 99.5% anhydrous citric acid; not > 5% water; not > 0.05% ash; not > 0.001% heavy metals; not > 0.0003% As. Hydrous citric acid may contain up to 8.8% water [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984., p. V6: 160 (1979)]**PEER REVIEWED**

Liquid citric acid is commercially available in a variety of concentrations with 50% w/w being most common. Grades are available that vary in appearance, purity, and color. [Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V6 366 (1993)]**PEER REVIEWED**

CONSUMPTION PATTERNS:

73% IN FOODS & BEVERAGES AS AN ACIDULANT, PH REGULATOR, FLAVOR ENHANCER, PRESERVATIVE, & ANTIOXIDANT SYNERGIST; 16% IN PHARMACEUTICAL PREPARATIONS PRINCIPALLY IN EFFERVESCENT ANTACID POWDERS & TABLETS; 11% IN METAL CLEANING & FINISHING, & AS A CHEMICAL INTERMEDIATE FOR ESTERS & SALTS FOR DETERGENTS & PLASTICIZERS. ) **PEER REVIEWED**

U. S. PRODUCTION:

This chemical is listed as a High Production Volume (HPV) (65FR81686). Chemicals listed as HPV were produced in or imported into the U.S. in > 1 million pounds in 1990 and/or 1994. The HPV list is based on the 1990 Inventory Update Rule. (IUR) (40 CFR part 710 subpart B; 51FR21438). [EPA/Office of Pollution Prevention and Toxics; High Production Volume (HPV) Challenge Program. Available from, as of May 17, 2006: http://www.epa.gov/opptintr/chemrtk/hpvchmlt.htm]**PEER REVIEWED**

(1990) Worldwide citric acid production: Western Europe 41.0%; North America 28.0%; Far East, Australia, and New Zealand 11.0%; South and Central America 9.0%; Remainder of the world 11.0%. /From table/ [Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V6 367 (1993)]**PEER REVIEWED**

... 1990 worldwide production estimated at approximately 550,000 metric tons. [Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V6 366 (1993)]**PEER REVIEWED**

(1972) 7.6X10+10 GRAMS (EST) **PEER REVIEWED**

(1976) 9.8X10+10 GRAMS (EST) **PEER REVIEWED**

(1986) > 100 million-500 million pounds [US EPA; Non-confidential Production Volume Information Submitted by Companies for Chemicals Under the 1986-2002 Inventory Update Rule (IUR). Citric acid (77-92-9). Available from, as of May 16, 2006: http://www.epa.gov/oppt/iur/iur02/search03.htm]**PEER REVIEWED**

(1990) > 100 million-500 million pounds [US EPA; Non-confidential Production Volume Information Submitted by Companies for Chemicals Under the 1986-2002 Inventory Update Rule (IUR). Citric acid (77-92-9). Available from, as of May 16, 2006: http://www.epa.gov/oppt/iur/iur02/search03.htm]**PEER REVIEWED**

(1991) 3.86X10+8 lb [SRI. 1992 Directory of Chemical Producers-United States of America. Menlo Park, CA: SRI International, 1992., p. 538]**PEER REVIEWED**

(1994) > 100 million-500 million pounds [US EPA; Non-confidential Production Volume Information Submitted by Companies for Chemicals Under the 1986-2002 Inventory Update Rule (IUR). Citric acid (77-92-9). Available from, as of May 16, 2006: http://www.epa.gov/oppt/iur/iur02/search03.htm]**PEER REVIEWED**

(1998) > 100 million-500 million pounds [US EPA; Non-confidential Production Volume Information Submitted by Companies for Chemicals Under the 1986-2002 Inventory Update Rule (IUR). Citric acid (77-92-9). Available from, as of May 16, 2006: http://www.epa.gov/oppt/iur/iur02/search03.htm]**PEER REVIEWED**

(2002) > 100 million-500 million pounds [US EPA; Non-confidential Production Volume Information Submitted by Companies for Chemicals Under the 1986-2002 Inventory Update Rule (IUR). Citric acid (77-92-9). Available from, as of May 16, 2006: http://www.epa.gov/oppt/iur/iur02/search03.htm]**PEER REVIEWED**

U. S. IMPORTS:

(1972) 1.46X10+8 GRAMS **PEER REVIEWED**

(1975) 3.4X10+8 GRAMS **PEER REVIEWED**

(1985) 1.96X10+10 g [BUREAU OF THE CENSUS. U.S. IMPORTS FOR CONSUMPTION AND GENERAL IMPORTS 1985 p.1-577]**PEER REVIEWED**

U. S. EXPORTS:

(1972) 4.94X10+9 GRAMS **PEER REVIEWED**

(1975) 4.2X10+9 GRAMS **PEER REVIEWED**

(1985) 6.71X10+9 g [BUREAU OF THE CENSUS. U.S. EXPORTS, SCHEDULE E, 1985 p.2-78]**PEER REVIEWED**

LABORATORY METHODS:

ANALYTIC LABORATORY METHODS:

ENZYMIC, GLC, AND HPLC METHODS FOR DETERMINING SUGARS AND ORGANIC ACIDS IN STRAWBERRIES ARE COMPARED. [REYES FG R ET AL; J ASSOC OFF ANAL CHEM 65 (1): 126 (1982)]**PEER REVIEWED**

Determination of citric acid by using LC equipped with a refractive index detector. Flow rate is about 0.6 ml/min. [USP Convention. The United States Pharmacopeia XXII/National Formulary XVII. Rockville, MD: United States Pharmacopeial Convention, Inc., 1990., p. 315]**PEER REVIEWED**

Method: AOAC 986.13; Procedure: liquid chromatographic method; Analyte: citric acid; Matrix: cranberry juice cocktail and apple juice; Detection Limit: not provided. [Horwitz W, ed.; Official Methods of Analysis of AOAC International 17th ed. (2003). CD-ROM, AOAC International, Gaithersburg, MD ]**PEER REVIEWED**

Method: AOAC 985.11; Procedure: enzymatic method; Analyte: citric acid; Matrix: wine; Detection Limit: not provided. [Horwitz W, ed.; Official Methods of Analysis of AOAC International 17th ed. (2003). CD-ROM, AOAC International, Gaithersburg, MD ]**PEER REVIEWED**

Method: AOAC 976.15; Procedure: colorimetric method; Analyte: citric acid; Matrix: cheese; Detection Limit: not provided. [Horwitz W, ed.; Official Methods of Analysis of AOAC International 17th ed. (2003). CD-ROM, AOAC International, Gaithersburg, MD ]**PEER REVIEWED**

Method: AOAC 932.05; Procedure: gravimetric method; Analyte: citric acid; Matrix: milk; Detection Limit: not provided. [Horwitz W, ed.; Official Methods of Analysis of AOAC International 17th ed. (2003). CD-ROM, AOAC International, Gaithersburg, MD ]**PEER REVIEWED**

Method: AOAC 920.126; Procedure: gravimetric method; Analyte: citric acid; Matrix: cheese; Detection Limit: not provided. [Horwitz W, ed.; Official Methods of Analysis of AOAC International 17th ed. (2003). CD-ROM, AOAC International, Gaithersburg, MD ]**PEER REVIEWED**

An enzymatic method, which is specific for the citrate moiety, can be used as a combined assay and identification test for citric acid and its common salts down to 20 ppm. [Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V6 368 (1993)]**PEER REVIEWED**

A high performance liquid chromatography (hplc) method to determine citric acid and other organic acids has been developed. The method is an isocratic system using sulfuric acid to elute organic acids onto a specific hplc column. The method is sensitive for citric acid down to ppm levels and is capable of quantifying citric acid in clear aqueous systems. [Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V6 368 (1993)]**PEER REVIEWED**

Analyte: citric acid; matrix: chemical identification; procedure: infrared absorption spectrophotometry with comparison to standards /anhydrous citric acid/ [U.S. Pharmacopeia. The United States Pharmacopeia, USP 29/The National Formulary, NF 24; Rockville, MD: U.S. Pharmacopeial Convention, Inc., p523 (2006) ]**PEER REVIEWED**

Analyte: citric acid; matrix: chemical purity; dissolution in water;

addition of phenolphthalein indicator; titration with sodium hydroxide /anhydrous citric acid/ [U.S. Pharmacopeia. The United States Pharmacopeia, USP 29/The National Formulary, NF 24; Rockville, MD: U.S. Pharmacopeial Convention, Inc., p523 (2006) ]**PEER REVIEWED**

SPECIAL REFERENCES:

SPECIAL REPORTS:

Leung HW, Paustenbach DJ; Organic Acids and Bases: Review of Toxicological Studies; Am J Ind Med 18 (6): 717-35 (1990).

USEPA/Office of Pesticide Programs; Reregistration Eligibility Decision Document - Citric Acid (June 1992). Available from the Database Query page at http://cfpub.epa.gov/oppref/rereg/status.cfm?show=rereg as of June 21, 2006. The RED summarizes the risk assessment conclusions and outlines any risk reduction measures necessary for the pesticide to continue to be registered in the U.S. [ ]

SYNONYMS AND IDENTIFIERS:

SYNONYMS:

USEPA/OPP Pesticide Code: 21801 [National Pesticide Informaton Retrieval System's USEPA/OPP Chemical Ingredients Database on Citric acid (77-92-9). Available from, as of April 20, 2006: http://ppis.ceris.purdue.edu/htbin/epachem.com]**PEER REVIEWED**

ACILETTEN [Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 955]**PEER REVIEWED**

ANHYDROUS CITRIC ACID [U.S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety Health. Registry of Toxic Effects of Chemical Substances (RTECS). National Library of Medicine's current MEDLARS file., p. 82/7908]**PEER REVIEWED**

Citralite [Milne, G.W.A. Veterinary Drugs: Synonyms and Properties. Ashgate Publishing Limited, Aldershot, Hampshire, England 2002., p. 155]**PEER REVIEWED**

CITRETTEN [Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 955]**PEER REVIEWED**

CITRIC ACID, ANHYDROUS [U.S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety Health. Registry of Toxic Effects of Chemical Substances (RTECS). National Library of Medicine's current MEDLARS file., p. 82/7908]**PEER REVIEWED**

CITRO [Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 955]**PEER REVIEWED**

FEMA NUMBER 2306 [Fenaroli's Handbook of Flavor Ingredients. Volume 2. Edited, translated, and revised by T.E. Furia and N. Bellanca. 2nd ed. Cleveland: The Chemical Rubber Co., 1975., p. 101]**PEER REVIEWED**

Hydrocerol a [Milne, G.W.A. Veterinary Drugs: Synonyms and Properties. Ashgate Publishing Limited, Aldershot, Hampshire, England 2002., p. 155]**PEER REVIEWED**

2-HYDROXYPROPANETRICARBOXYLIC ACID [Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 955]**PEER REVIEWED**

2-HYDROXY-1,2,3-PROPANETRICARBOXYLIC ACID [O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition, Whitehouse Station, NJ: Merck and Co., Inc., 2001., p. 405]**PEER REVIEWED**

BETA-HYDROXYTRICARBALLYLIC ACID [U.S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety Health. Registry of Toxic Effects of Chemical Substances (RTECS). National Library of Medicine's current MEDLARS file., p. 82/7908]**PEER REVIEWED**

2-HYDROXYTRICARBALLYLIC ACID [Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 955]**PEER REVIEWED**

BETA-HYDROXY-TRICARBOXYLIC ACID [U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5., p. ]**PEER REVIEWED**

KYSELINA CITRONOVA (CZECH) [U.S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety Health. Registry of Toxic Effects of Chemical Substances (RTECS). National Library of Medicine's current MEDLARS file., p. 82/7908]**PEER REVIEWED**

ASSOCIATED CHEMICALS: Citric acid monohydrate;5949-29-1

FORMULATIONS/PREPARATIONS:

... Anticoagulant citrate dextrose solution, anticoagulant citrate phosphate dextrose solution, citric acid syrup, & effervescent salts. [Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975., p. 1260]**PEER REVIEWED**

Grades of purity: USP; reagent; monohydrate grade. [U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5., p. ]**PEER REVIEWED**

Grades: Both hydrous (hydrated) and anhydrous, Technical, Chemically Pure, United States Pharmacopeia, Food Chemical Codex. [Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 14th Edition. John Wiley & Sons, Inc. New York, NY 2001., p. 272]**PEER REVIEWED**

Citric acid for pharmaceutical use: not < 99.5% anhydrous citric acid; not > 5% water; not > 0.05% ash; not > 0.001% heavy metals; not > 0.0003% As. Hydrous citric acid may contain up to 8.8% water [Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984., p. V6: 160 (1979)]**PEER REVIEWED**

Liquid citric acid is commercially available in a variety of concentrations with 50% w/w being most common. Grades are available that vary in appearance, purity, and color. [Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. Volumes 1: New York, NY. John Wiley and Sons, 1991-Present., p. V6 366 (1993)]**PEER REVIEWED**

ADMINISTRATIVE INFORMATION:

HAZARDOUS SUBSTANCES DATABANK NUMBER: 911

LAST REVISION DATE: 20061220

LAST REVIEW DATE: Reviewed by SRP on 9/14/2006

UPDATE HISTORY:

Complete Update on 2006-12-20, 56 fields added/edited/deleted

Complete Update on 03/05/2003, 1 field added/edited/deleted.

Field Update on 08/06/2002, 1 field added/edited/deleted.

Field Update on 01/14/2002, 1 field added/edited/deleted.

Field Update on 08/08/2001, 1 field added/edited/deleted.

Complete Update on 08/26/1999, 1 field added/edited/deleted.

Complete Update on 06/03/1999, 1 field added/edited/deleted.

Complete Update on 02/27/1998, 1 field added/edited/deleted.

Complete Update on 10/20/1997, 1 field added/edited/deleted.

Complete Update on 04/07/1997, 2 fields added/edited/deleted.

Complete Update on 03/12/1997, 1 field added/edited/deleted.

Complete Update on 06/06/1996, 1 field added/edited/deleted.

Complete Update on 01/19/1996, 1 field added/edited/deleted.

Complete Update on 05/26/1995, 1 field added/edited/deleted.

Complete Update on 12/22/1994, 1 field added/edited/deleted.

Complete Update on 10/19/1994, 1 field added/edited/deleted.

Complete Update on 04/16/1994, 55 fields added/edited/deleted.

Field Update on 03/21/1994, 1 field added/edited/deleted.

Field update on 12/16/1992, 1 field added/edited/deleted.

Complete Update on 10/10/1990, 1 field added/edited/deleted.

Complete Update on 04/16/1990, 1 field added/edited/deleted.

Field update on 12/29/1989, 1 field added/edited/deleted.

Complete Update on 03/04/1988, 8 fields added/edited/deleted.

Created 19830315 by SYS

# SAFETY DATA SHEET

according to Regulation (EC) No. 1907/2006
Version 4.0 Revision Date 19.07.2010
Print Date 02.08.2010
GENERIC EU MSDS - NO COUNTRY SPECIFIC DATA - NO OEL DATA

## 1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

| | | |
|---|---|---|
| Product name | : | Citric acid |
| Product Number | : | 240621 |
| Brand | : | Sigma-Aldrich |
| Company | : | Sigma-Aldrich Chemie GmbH<br>Riedstrasse 2<br>D-89555 STEINHEIM |
| Telephone | : | +4989651301444 |
| Fax | : | +497329972319 |
| Emergency Phone # | : | +49 7329-97-2323 |
| E-mail address | : | eurtechserv@sial.com |

## 2. HAZARDS IDENTIFICATION

### Classification of the substance or mixture

According to Regulation (EC) No1272/2008
Skin irritation (Category 2)
Serious eye damage (Category 1)

According to European Directive 67/548/EEC as amended.
Risk of serious damage to eyes.

### Label elements

Pictogram

Signal word Danger

Hazard statement(s)
H315 Causes skin irritation.
H318 Causes serious eye damage.

Precautionary statement(s)
P280 Wear protective gloves/eye protection/face protection.
P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

Hazard symbol(s)
Xi Irritant

R-phrase(s)
R41 Risk of serious damage to eyes.

S-phrase(s)
S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
S39 Wear eye/face protection.

**Other hazards** - none

## 3. COMPOSITION/INFORMATION ON INGREDIENTS

Formula : $C_6H_8O_7$
Molecular Weight : 192,12 g/mol

| CAS-No. | EC-No. | Index-No. | Classification | Concentration |
|---|---|---|---|---|
| **Citric acid** | | | | |
| 77-92-9 | 201-069-1 | - | Eye Dam. 1; H318<br>Xi, R41 | - |

For the full text of the H-Statements mentioned in this Section, see Section 16.

## 4. FIRST AID MEASURES

**General advice**
Consult a physician. Show this safety data sheet to the doctor in attendance.

**If inhaled**
If breathed in, move person into fresh air. If not breathing, give artificial respiration. Consult a physician.

**In case of skin contact**
Wash off with soap and plenty of water. Consult a physician.

**In case of eye contact**
Rinse thoroughly with plenty of water for at least 15 minutes and consult a physician.

**If swallowed**
Never give anything by mouth to an unconscious person. Rinse mouth with water. Consult a physician.

## 5. FIRE-FIGHTING MEASURES

**Suitable extinguishing media**
Use water spray, alcohol-resistant foam, dry chemical or carbon dioxide.

**Special protective equipment for fire-fighters**
Wear self contained breathing apparatus for fire fighting if necessary.

## 6. ACCIDENTAL RELEASE MEASURES

**Personal precautions**
Use personal protective equipment. Avoid dust formation. Avoid breathing vapors, mist or gas. Ensure adequate ventilation. Evacuate personnel to safe areas. Avoid breathing dust.

**Environmental precautions**
Do not let product enter drains.

**Methods and materials for containment and cleaning up**
Pick up and arrange disposal without creating dust. Sweep up and shovel. Keep in suitable, closed containers for disposal.

## 7. HANDLING AND STORAGE

**Precautions for safe handling**
Avoid contact with skin and eyes. Avoid formation of dust and aerosols.
Provide appropriate exhaust ventilation at places where dust is formed. Normal measures for preventive fire protection.

**Conditions for safe storage**
Keep container tightly closed in a dry and well-ventilated place. Store in cool place.

## 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

### Personal protective equipment

#### Respiratory protection
Where risk assessment shows air-purifying respirators are appropriate use a full-face particle respirator type N100 (US) or type P3 (EN 143) respirator cartridges as a backup to engineering controls. If the respirator is the sole means of protection, use a full-face supplied air respirator. Use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU).

#### Hand protection
Handle with gloves. Gloves must be inspected prior to use. Use proper glove removal technique (without touching glove's outer surface) to avoid skin contact with this product. Dispose of contaminated gloves after use in accordance with applicable laws and good laboratory practices. Wash and dry hands.

The selected protective gloves have to satisfy the specifications of EU Directive 89/686/EEC and the standard EN 374 derived from it.

#### Eye protection
Face shield and safety glasses Use equipment for eye protection tested and approved under appropriate government standards such as NIOSH (US) or EN 166(EU).

#### Skin and body protection
Complete suit protecting against chemicals, The type of protective equipment must be selected according to the concentration and amount of the dangerous substance at the specific workplace.

#### Hygiene measures
Handle in accordance with good industrial hygiene and safety practice. Wash hands before breaks and at the end of workday.

## 9. PHYSICAL AND CHEMICAL PROPERTIES

### Appearance

| | |
|---|---|
| Form | solid |

### Safety data

| | |
|---|---|
| pH | no data available |
| Melting point | 153 - 159 °C |
| Boiling point | no data available |
| Flash point | no data available |
| Ignition temperature | no data available |
| Lower explosion limit | 8 %(V) |
| Water solubility | no data available |

## 10. STABILITY AND REACTIVITY

#### Chemical stability
Stable under recommended storage conditions.

#### Conditions to avoid
no data available

#### Materials to avoid
Oxidizing agents, Bases, Reducing agents, Nitrates

#### Hazardous decomposition products
Hazardous decomposition products formed under fire conditions. - Carbon oxides

## 11. TOXICOLOGICAL INFORMATION

**Acute toxicity**
LD50 Oral - rat - 3.000 mg/kg

**Skin corrosion/irritation**
Skin - rabbit - Mild skin irritation - 24 h

**Serious eye damage/eye irritation**
Eyes - rabbit - Severe eye irritation - 24 h

**Respiratory or skin sensitization**
Prolonged or repeated exposure may cause allergic reactions in certain sensitive individuals.

**Germ cell mutagenicity**
no data available

**Carcinogenicity**

IARC: No component of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

**Reproductive toxicity**
no data available

**Specific target organ toxicity - single exposure**
no data available

**Specific target organ toxicity - repeated exposure**
no data available

**Aspiration hazard**
no data available

**Potential health effects**

| | |
|---|---|
| **Inhalation** | May be harmful if inhaled. Causes respiratory tract irritation. |
| **Ingestion** | May be harmful if swallowed. |
| **Skin** | May be harmful if absorbed through skin. Causes skin irritation. |
| **Eyes** | Causes eye burns. |

**Signs and Symptoms of Exposure**
Vomiting, Diarrhoea, Damage to tooth enamel., Dermatitis, To the best of our knowledge, the chemical, physical, and toxicological properties have not been thoroughly investigated.

**Additional Information**
RTECS: GE7350000

## 12. ECOLOGICAL INFORMATION

**Toxicity**

| | |
|---|---|
| Toxicity to fish | LC50 - Leuciscus idus melanotus - 440 mg/l - 48 h |

**Persistence and degradability**
no data available

**Bioaccumulative potential**
no data available

**Mobility in soil**
no data available

**PBT and vPvB assessment**
no data available

**Other adverse effects**
no data available

## 13. DISPOSAL CONSIDERATIONS

**Product**
Offer surplus and non-recyclable solutions to a licensed disposal company. Contact a licensed professional waste disposal service to dispose of this material. Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.

**Contaminated packaging**
Dispose of as unused product.

## 14. TRANSPORT INFORMATION

**ADR/RID**
Not dangerous goods

**IMDG**
Not dangerous goods

**IATA**
Not dangerous goods

## 15. REGULATORY INFORMATION

This safety datasheet complies with the requirements of Regulation (EC) No. 1907/2006.

## 16. OTHER INFORMATION

**Text of H-code(s) and R-phrase(s) mentioned in Section 3**

| | |
|---|---|
| Eye Dam. | Serious eye damage |
| H318 | Causes serious eye damage. |
| Xi | Irritant |
| R41 | Risk of serious damage to eyes. |

**Further information**

The above information is believed to be correct but does not purport to be all inclusive and shall be used only as a guide. The information in this document is based on the present state of our knowledge and is applicable to the product with regard to appropriate safety precautions. It does not represent any guarantee of the properties of the product. Sigma-Aldrich Co., shall not be held liable for any damage resulting from handling or from contact with the above product. See reverse side of invoice or packing slip for additional terms and conditions of sale.