AR201-13952A

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ROBUST SUMMARY FOR GLYCOLIC ACID

Summary

Glycolic acid is a colorless, odorless, crystalline solid, but is usually supplied as a 70% solution. In this form it is a clear, colorless liquid with a mild odor. As a 70% solution, it has a saturation point of 10°C, boiling point of 112°C, and is non-flammable.

The Henry's Law constant for glycolic acid is estimated to be 8.5×10^{-8} atm-m^3/mole, therefore glycolic acid will not volatilize rapidly from water surfaces. The estimated half-life from a river is 373.8 days and 2721 days from a model lake based on volatilization alone, with no accounting for biodegradation. If discharged into water, it is estimated that glycolic acid will partition predominately in the water compartment. Glycolic acid biodegrades quickly, with and without acclimation using a variety of microbial inoculum. Accordingly, glycolic acid is not expected to biopersist or bioaccumulate in the environment.

Glycolic acid exhibits low toxicity to aquatic organisms. Based on measured test concentrations, the following endpoint values have been reported: 96-hour LC_{50} with fathead minnows of 168 ppm and 48-hour EC_{50} with *Daphnia* of 141 mg/L. Glycolic acid caused stimulation of algal growth at pH 7.5 under illumination, but when used as a carbon source, did not support heterotrophic growth in the dark.

Glycolic acid (70% solution) is slightly toxic via the oral route, having an LD_{50} in rats of 1938 mg/kg. It is moderately toxic via the inhalation route in male rats with a 4-hour LC_{50} of 3.6 mg/L. Glycolic acid is a skin and eye corrosive, but it is not a skin sensitizer in animals. However, numerous studies in humans with cosmetic products containing lower percentages of glycolic acid have shown some skin irritation potential, but no corrosivity. Repeated exposures to glycolic acid via inhalation produced liver, spleen, thymus changes, and gastrointestinal tract alterations. Repeated administration of glycolic acid to rats by oral intubation caused decreases in body weight, body weight gain, food consumption, and food efficiency. In addition, toxicologically significant changes in hematologic measurements, clinical chemistry, and urinalysis parameters, as well as kidney lesions were observed. Maternal and developmental toxicity of crystalline, 99.6% pure, glycolic acid in the rat was seen at 300 and 600 mg/kg/day. The maternal and developmental NOEL was 150 mg/kg/day, thus glycolic acid is not considered a unique developmental hazard to the conceptus. Glycolic acid did not affect reproductive performance in rats during a one-generation reproduction study following a 90-day feeding study. The compound was negative in the *in vitro* bacterial reverse mutation assay (*Salmonella* and *E. coli*). Glycolic acid produced a positive response in the *in vitro* mouse lymphoma assay only at excessively high concentrations under activated conditions, but was negative in the *in vivo* mouse micronucleus assay.

General Exposure Information

Glycolic acid is an α-hydroxy acid that occurs widely in nature. It is present in several edible fruits, vegetables, and beverages at concentrations ranging up to approximately 56 ppm. Most commercially used glycolic acid, however, is manufactured through various processes involving

chemical synthesis. The annual U.S. market of 25–30 million lbs. is primarily supplied through domestic production, with imports accounting for approximately 5% of sales.

Glycolic acid is primarily used in a broad range of industrial products, but it also finds application in a few consumer formulations. Applications include removal of mineral scale, acidity control (pH adjustment), water treatment, intermediate in chemical synthesis, and personal care products. Most applications start with glycolic acid as an approximate 70% aqueous solution, which is diluted significantly for the end-use.

Approximate applications as a percentage of sales volume are: household, institutional, and industrial cleaning = 35%; chemicals manufacture = 18%; pH control = 11%; electronics applications = 7%; textile applications = 5%; metal finishing = 4%; oil and gas treatment = 4%; water treatment = 2%; and miscellaneous = 14%. Miscellaneous applications include leather and paper manufacture, laundry aid component, additive in adhesives, and personal care products (primarily facial creams). Glycolic acid is an FDA-approved indirect food additive. The amount of glycolic acid used in these applications varies from about 0.2% to about 30% of the final product weight. The range is widest in the industrial, household, and institutional cleaning segment (0.2-20%).

Exposure through natural occurrence: Glycolic acid is naturally present in a variety of fruits, vegetables, meats, and beverages in concentrations ranging from approximately 0.5-5.6 mg/100 g (vegetables), approximately 5-50 mg/kg (fruits), 1–5 mg/kg (beef and chicken), and approximately 0.5-30 mg/kg (various common non-alcoholic beverages). The dietary intake of glycolic acid from these sources is estimated to be about 1.0 mg/kg/day.

Exposure during manufacture: Glycolic acid is manufactured in closed systems where reactors and downstream equipment are hard-piped, to minimize both losses to the environment and potential exposure to workers. Routine air monitoring in DuPont facilities indicate workplace concentrations to average <0.4 mg/m^3, 8-hour time weighted average (TWA). Continuous exposure at this level for an entire 8-hour shift would correspond to a daily intake of <0.04 mg/kg/day. Glycolic acid is normally packaged and sold in drums or in bulk. Air monitoring of drumming and bulk loading operations show typical exposure levels to be <0.2 and <0.4 mg/m^3, respectively. This would correspond to an intake of <0.02 and <0.04 mg/kg/day for exposed workers, assuming continuous exposure at these levels for an entire 8-hour shift.

Exposure during use (product formulation): In the majority of glycolic acid applications, customers blend the chemical with other ingredients. Typical air monitoring data from household cleaner and personal care production operations, most of which involve partially enclosed manufacturing systems, show levels below 0.10 mg/m^3, 8-hour TWA. This corresponds to a daily intake of <0.01 mg/kg/day for exposed workers.

Exposure during use (household or institutional cleaner use): Bathroom soap scum cleaners containing glycolic acid are typically applied using a hand pump spray followed by wiping and rinsing. The typical estimated daily exposure to glycolic acid for workers handling these

products is about 0.06 mg/kg/day for household use and about 0.10 mg/kg/day for institutional use.

Based on the above, the dietary intake of glycolic acid from naturally occurring foods exceeds the intake that might result from exposure to the compound during manufacture and use in all industrial applications. DuPont's Acceptable Exposure Limit (AEL or safe exposure limit) for glycolic acid, which is based on an assessment of all available toxicity data on the compound, is 10 mg/m^3, 8- and 12-hour TWA.

Exposure during use (personal care applications): Glycolic acid formulations have been used by dermatologists for over 25 years for cosmetology and the treatment of a variety of skin disorders. In the last decade, glycolic acid has been included as a component in several over-the-counter personal care products, which include exfoliants, pH adjusters, and skin conditioning agents. Since the concentrations used, the condition and duration of use, and the pH range of these products span a broad spectrum, the estimation of overall or average exposure is infeasible. It is recognized, however, that the amount of glycolic acid systemically absorbed through the skin in 24 hours ranges from about 30% to 3% of the quantity applied for products ranging in pH from 3 to 7, respectively. While localized irritation at the site of application has been observed, no systemic toxicity has been noted as a result of these dermal applications. Several toxicity studies on a variety of these products by independent dermatologists and toxicologists have shown that glycolic acid is safe for personal care use when it is formulated and used within recommended pH limits and concentrations to minimize skin irritation.

TEST PLAN FOR GLYCOLIC ACID

Glycolic acid **CAS No. 79-14-1**	**Data Available**	**Data Acceptable**	**Testing Required**
	Y/N	**Y/N**	**Y/N**
PHYSICAL/CHEMICAL CHARACTERISTICS			
Melting Point	Y	Y	N
Boiling Point	Y	Y	N
Vapor Pressure	Y	Y	N
Partition Coefficient	Y	Y	N
Water Solubility	Y	Y	N
ENVIRONMENTAL FATE			
Photodegradation	Y	Y	N
Stability in Water	Y	Y	N
Transport (Fugacity)	Y	Y	N
Biodegradation	Y	Y	N
ECOTOXICITY			
Acute Toxicity to Fish	Y	Y	N
Acute Toxicity to Invertebrates	Y	Y	N
Acute Toxicity to Aquatic Plants	Y	Y	N
MAMMALIAN TOXICITY			
Acute Toxicity	Y	Y	N
Repeated Dose Toxicity	Y	Y	N
Developmental Toxicity	Y	Y	N
Reproductive Toxicity	Y	Y	N
Genetic Toxicity Gene Mutations	Y	Y	N
Genetic Toxicity Chromosomal Aberrations	Y	Y	N