

SCREENING-LEVEL HAZARD CHARACTERIZATION

Glycolic Acid (CASRN 79-14-1)

The High Production Volume (HPV) Challenge Program¹ was conceived as a voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsored chemicals; sponsorship entailed the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data did not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to “SIDS” (Screening Information Data Set^{1,2}) endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment.

The Environmental Protection Agency’s Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1400 sponsored chemicals by developing hazard characterizations (HCs). These HCs consist of an evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. They are not intended to be definitive statements regarding the possibility of unreasonable risk of injury to health or the environment.

The evaluation is performed according to established EPA guidance^{2,3} and is based primarily on hazard data provided by sponsors; however, in preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor’s responses to comments and revisions made to the submission. In order to determine whether any new hazard information was developed since the time of the HPV submission, a search of the following databases was made from one year prior to the date of the HPV Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, EXTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. OPPT’s focus on these specific sources is based on their being of high quality, highly relevant to hazard characterization, and publicly available.

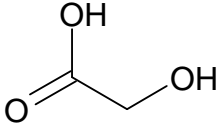
OPPT does not develop HCs for those HPV chemicals which have already been assessed internationally through the HPV program of the Organization for Economic Cooperation and Development (OECD) and for which Screening Initial Data Set (SIDS) Initial Assessment Reports (SIAR) and SIDS Initial Assessment Profiles (SIAP) are available. These documents are presented in an international forum that involves review and endorsement by governmental authorities around the world. OPPT is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments.

¹ U.S. EPA. High Production Volume (HPV) Challenge Program; <http://www.epa.gov/chemrtk/index.htm>.

² U.S. EPA. HPV Challenge Program – Information Sources; <http://www.epa.gov/chemrtk/pubs/general/guidocs.htm>.

³ U.S. EPA. Risk Assessment Guidelines; <http://cfpub.epa.gov/ncea/raf/rafguid.cfm>.

These hazard characterizations are technical documents intended to inform subsequent decisions and actions by OPPT. Accordingly, the documents are not written with the goal of informing the general public. However, they do provide a vehicle for public access to a concise assessment of the raw technical data on HPV chemicals and provide information previously not readily available to the public.

<p>Chemical Abstract Service Registry Number (CASRN)</p>	<p>79-14-1</p>
<p>Chemical Abstract Index Name</p>	<p>Acetic acid, hydroxyl-</p>
<p>Structural Formula</p>	
<p style="text-align: center;">Summary</p> <p>CASRN 79-14-1 is a colorless crystalline solid (the commercial products are often supplied as a 70% aqueous solution) with high water solubility and moderate vapor pressure. It is expected to have high mobility in soil. Volatilization is considered negligible since CASRN 79-14-1 will exist as an anion under environmental conditions and anions do not volatilize. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered slow. CASRN 79-14-1 is expected to have low persistence (P1) and low bioaccumulation potential (B1).</p> <p>The acute toxicity of CASRN 79-14-1 in rats is low by the oral route and moderate by the inhalation route. A 90-day oral gavage repeated-dose toxicity study in rats showed kidney effects (histopathology) and changes in hematology and clinical chemistry changes in males at 300 mg/kg-day and higher; the NOAEL for systemic toxicity is 150 mg/kg-day. A 14-day inhalation repeated-dose toxicity study in rats showed extreme morbidity, decreased body weight, alterations in clinical chemistry and urinalysis parameters, and effects on the thymus, liver, spleen and kidney at 0.51 mg/L/day; the NOAEC for systemic toxicity is 0.16 mg/L/day. In the reproductive toxicity subset of the 90-day oral repeated-dose toxicity study, kidney effects were reported in males at 600 mg/kg-day and decreases in body weight were reported in females at 300 mg/kg-day; the NOAEL for systemic toxicity in males and females is 300 and 150 mg/kg-day, respectively. No treatment-related effects were observed on any of the reproductive parameters measured; the NOAEL for reproductive toxicity is 600 mg/kg-day, the highest dose tested. In an oral prenatal developmental toxicity study with CASRN 79-14-1 in rats, maternal effects included significant reductions in body weight and food consumption, abnormal gait/staggering, lung noise, irregular respiration and lethargy at 300 mg/kg-day; the NOAEL for maternal toxicity is 150 mg/kg-day. Malformations and variations were observed in the fetuses at 300 mg/kg-day; the NOAEL for developmental is 150 mg/kg-day. CASRN 79-14-1 was not mutagenic to bacterial cells, but was mutagenic in mammalian cells <i>in-vitro</i>. CASRN 79-14-1 did not induce formation of micronuclei in mice <i>in-vivo</i>. CASRN 79-14-1 was irritating to rabbit skin and eyes but did not cause skin sensitization in guinea pigs.</p> <p>For CASRN 79-14-1, the 96-hour LC₅₀ for fish is 164 mg/L (nominal). The 48-hour EC₅₀ for aquatic invertebrates is 141 mg/L (nominal). The 72-hour EC₅₀ for aquatic plants is 44 mg/L (measured) for growth and 21.6 mg/L (measured) for biomass.</p>	

There are no data gaps identified under the HPV Challenge Program.

The sponsor, DuPont Company, submitted a Test Plan and Robust Summaries to EPA for glycolic acid (CAS No. 79-14-1; CA index name: acetic acid, hydroxyl-) on July 17, 2001. EPA posted the submission on the ChemRTK HPV Challenge website on August 17, 2001 (<http://www.epa.gov/hpv/pubs/summaries/glyclacd/c13125tc.htm>). EPA comments on the original submission were posted to the website on February 13, 2002. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on April 4, 2002 which were posted to the ChemRTK website on April 23, 2002 and September 24, 2002.

1. Chemical Identity

1.1 Identification and Purity

The following description is taken from the 2002 Test Plan and Robust Summary:

CASRN 79-14-1 is a colorless crystalline solid with high water solubility and moderate vapor pressure. The commercial products are usually supplied as a 70% clear, colorless aqueous solution. Purity of the test substance, when noted in the Robust Summary, was >98%.

1.2 Physical-Chemical Properties and Environmental Fate

The physical-chemical properties of CASRN 79-14-1 are summarized in Table 1, while its environmental fate properties are provided in Table 2.

Table 1. Physical-Chemical Properties of CASRN 79-14-1¹	
Property	Value
CASRN	79-14-1
Molecular Weight	76.05
Physical State	Colorless crystalline solid
Melting Point	78–79°C (measured)
Boiling Point	Decomposes at >100°C
Vapor Pressure	0.017 mm Hg at 25°C (measured)
Water Solubility	2.44×10 ⁶ mg/L at 25°C (measured: equivalent to 70% in water)
Dissociation Constant (pK _a)	3.83 (measured) ²
Henry's Law Constant	8.2×10 ⁻¹⁰ atm·m ³ /mole (estimated) ³
Log K _{ow}	-1.11 at 19°C (measured)

¹DuPont Company. April 2, 2002. Revised Test Plan and Robust Summary for Glycolic Acid. Available online from: <http://www.epa.gov/chemrtk/pubs/summaries/glyclacd/c13125tc.htm> as of March 22, 2010.

²SRC. 2010. The Physical Properties Database (PHYSPROP). SRC: Syracuse, NY. Available online from: <http://www.srcinc.com/what-we-do/free-demos.aspx> as of March 22, 2010.

³U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: <http://www.epa.gov/opptinr/exposure/pubs/episuitedl.htm> as of March 22, 2010.

2. General Information on Exposure

2.1 Production Volume and Use Pattern

According to the 2006 IUR submissions, CASRN 79-14-1 had an aggregated production and/or import volume in the United States between 10 and 50 million pounds.

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include other basic organic chemical manufacturing as intermediates, stabilizers, solvents (for cleaning or degreasing) and not readily obtainable (NRO); soap and cleaning compound manufacturing as solvents (for cleaning or degreasing); steam and air conditioning supply as solvents (for cleaning or degreasing); toilet preparation manufacturing as oxidizing agents; other chemical and allied products merchant wholesalers as not readily obtainable (NRO); and poured concrete foundation and structure contractors as solvents (for cleaning or degreasing). Non-confidential commercial and consumer uses of this chemical include polishes and sanitation goods.

2.2 Environmental Exposure and Fate

CASRN 79-14-1 is expected to have high mobility in soil. CASRN 79-14-1 was readily biodegradable using a closed bottle test (OECD 301D) and a modified MITI test (OECD 301C), achieving close to 90% mineralization in less than 2 weeks. The rate of volatilization is considered negligible since CASRN 79-14-1 is an acid that will exist as an anion under environmental conditions and anions do not volatilize. The rate of hydrolysis is considered negligible. CASRN 79-14-1 is expected to have low persistence (P1) and low bioaccumulation potential (B1).

Property	Value
Photodegradation Half-life	3.4 days (estimated) ²
Hydrolysis Half-life	Stable
Biodegradation	89.6% after 7 days (readily biodegradable); 86% after 14 days (readily biodegradable) ³
Bioaccumulation Factor	BAF = 0.9 (estimated) ²
Log K _{oc}	0 (estimated) ²
Fugacity (Level III Model) ²	
Air (%)	<0.1
Water (%)	33.5
Soil (%)	66.4
Sediment (%)	<0.1
Persistence ⁴	P1 (low)
Bioaccumulation ⁴	B1 (low)

¹DuPont Company. April 2, 2002. Revised Test Plan and Robust Summary for Glycolic Acid. Available online from: <http://www.epa.gov/chemrtk/pubs/summaries/glyclacd/c13125tc.htm> as of March 22, 2010.

²U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: <http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm> as of March 22, 2010.

³National Institute of Technology and Evaluation. 2002. Biodegradation and Bioaccumulation of the Existing Chemical Substances under the Chemical Substances Control Law. Available online from: http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html. As of March 22, 2010.

⁴Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

Conclusion: CASRN 79-14-1 is a colorless crystalline solid (the commercial products are often supplied as a 70% aqueous solution) with high water solubility and moderate vapor pressure. It is expected to have high mobility in soil. Volatilization is considered negligible since CASRN 79-14-1 will exist as an anion under environmental conditions and anions do not volatilize. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered slow. CASRN 79-14-1 is expected to have low persistence (P1) and low bioaccumulation potential (B1).

3. Human Health Effects

A summary of health effects data submitted for SIDS endpoints is provided in Table 3. The Agency notes that the animal studies suggest that males appear to be more susceptible than females to glycolic acid toxicity.

Acute Oral Toxicity

CrI:CD (SD)IGS BR rats (5/sex/dose) were administered doses of 1000, 2000 or 3000 mg/kg-bw of a 70% solution of the test substance by oral gavage and observed for 15 days. Mortality rates were 0/5, 2/5 and 5/5 for male rats and 0/5, 4/5 and 4/5 for female rats. Deaths occurred up to 4 days after dosing.

LD₅₀ = 1938 mg/kg-bw

Acute Inhalation Toxicity

Sprague-Dawley rats (5/sex) were exposed, nose-only, to 5.2 mg/L of the test substance for 4 hours. Additional groups of male rats (10/concentration) were exposed to 0.60, 2.1 or 3.8 mg/L for 4 hours. Chamber atmospheres were generated by aerosolization of the test substance using a nebulizer. The mass median aerodynamic diameter of the aerosol generated during the exposures was 2.3–3.1 µm. Mortality rates in male rats were 0/10, 2/10, 6/10 and 3/5 at 0.60, 2.1, 3.8 and 5.2 mg/L, respectively. The mortality rate for female rats was 0/5 at 5.2 mg/L. Mortality occurred during exposure or within 12 days following exposure.

LC₅₀ (male) = 3.6 mg/L

LC₅₀ (female) > 5.2 mg/L

Repeated-Dose Toxicity

Oral

Sprague-Dawley rats (40/sex/dose) were administered 0, 150, 300 or 600 mg/kg-day of the test substance diluted in water by gavage for 90 days. Each dose group was divided into subchronic toxicity, immunotoxicity, neurotoxicity and reproductive toxicity subsets (10 animals/sex/subset/dose) – results for each of these are described later in this Hazard Characterization. Outcomes assessed in the subchronic toxicity study included: body weight, food consumption, food efficiency, ophthalmic examination, clinical signs, organ weights, hematology, urinalysis, clinical chemistry, histopathology and survival. Complete histopathologic examination was performed in animals from the control and high-dose group; however, only liver kidney and lungs and “most gross lesions” were examined in the intermediate dose group, and no tissues were examined microscopically from the low dose group. Two compound-related deaths occurred in males at 600 mg/kg-day. No other compound-related mortality was observed in this study. Decreased mean body weight, overall body weight gain, food consumption and food efficiency occurred in males and females of the 300 and 600 mg/kg-day groups. These effects were considered adverse in the high dose group only (no further details provided). The robust summary further reported “toxicologically significant” increases in blood neutrophils, urea nitrogen, phosphorous and creatinine, and decreases in urine concentration in males at 300 and 600 mg/kg-day. Mean absolute and relative kidney weights were increased in mid- and high-dose male rats. Gross findings of renal pelvis dilation,

microscopic findings of oxalate crystal nephrosis and unilateral hydronephrosis, and hyperplasia of the transitional epithelium of the renal pelvis (considered secondary to irritation) were also observed (in males only) at these dose levels. No organ weight, gross or microscopic findings indicative of systemic toxicity were observed in female rats exposed to 300 or 600 mg/kg-day. Finally, microscopic findings (not specified) were observed in the respiratory tract (upper airways and lungs) of all treated animals and were thought to be a result of irritation from aspiration of glycolic acid following exposure via gavage.

LOAEL = 300 mg/kg-day (based on increased kidney weight and histopathology, alterations in hematology, clinical chemistry, and urinalysis – all in males)

NOAEL = 150 mg/kg-day

Inhalation

Sprague-Dawley rats (10 males/group) were exposed, nose-only, to concentrations of 0, 0.16, 0.51 or 1.4 mg/L of the test substance for 6 hours/day, 5 days/week for 2 weeks. After the exposure period, half of the animals were sacrificed and the remaining half remained on study for a two-week recovery period. Outcomes assessed included body weight, clinical signs, hematology, blood and urine clinical chemistry, organ weights and histopathology, and survival. Although there were no mortalities, one mid-concentration animal and seven high-concentration animals were sacrificed *in extremis*. Statistically significant and severe weight loss was observed throughout the exposure and recovery periods in mid- and high-concentration animals. Clinical signs of toxicity were observed in many animals in the mid and high concentration groups and included: labored breathing, lung noise, ruffled fur, red and clear nasal and ocular discharges, poor muscle tone and pallor. The incidence of the respiratory tract effects (e.g., lung noise, labored breathing and nasal discharge) ranged from 60 to 100% in the mid- and high-concentration group, 10% (1 of 10) in the low-concentration group, and 0% in the control group. Increased serum aspartate aminotransferase and decreased urine volume were observed in the mid-concentration group and had not resolved by the end of the recovery period. Decreased serum protein, increased alanine and aspartate aminotransferases and decreased urine volume and pH were observed in the high-concentration group, and were resolved by the end of the recovery period. Gross pathological changes were observed after the exposure period in the high-concentration group only and included distended GI tract, small spleen and small thymus. No gross effects were observed after the recovery period. Microscopically, mild, diffuse hepatocellular degeneration was detected in 1/10 (0/5 post-exposure, 1/5 following-recovery), 9/10 (5/5 post-exposure, 4/5 post-recovery) and 7/10 (at sacrifice) rats at 0.16, 0.51 and 1.4 mg/L, respectively. Atrophy and degeneration of the thymus were noted in 5/10 mid-concentration (2/5 post-exposure and 3/5 post-recovery) and 8/10 high-concentration (at sacrifice) rats. Absolute liver, spleen, kidney and thymus weights were significantly decreased in mid- and high-concentration rats. Relative lung weight was increased in low-concentration males.

Relative lung, liver, kidney and thymus weights were decreased in mid-concentration males.

LOAEC = 0.51 mg/L/day (based on extreme morbidity, decreased body weight, alterations in clinical chemistry and urinalysis parameters, effects on the thymus, liver, spleen and kidney)

NOAEC = 0.16 mg/L/day

Reproductive Toxicity

In the 90-day oral gavage repeated-dose toxicity study described previously, a group of animals (10/sex/dose) were allowed to mate within their treatment group starting on day 97. The animals were followed through birth and for an additional 21 days. The exposure period in the robust summary is defined as 90-days of feeding plus 1-generation reproduction; however, it is not clear if the animals were exposed to glycolic acid during the reproductive portion of the study. No treatment-related effects were reported for gestation length, mating index, fecundity index, gestation index, litter size, litter survival, implantation site numbers, implantation efficiency, sex ratio, percent pups born alive, pup survival, viability index, pup body weight, pup clinical signs, lactation index, or gross pathology and weight of the reproductive organs. Compound-related gross and microscopic lesions of the kidney were observed in male rats exposed to 600 mg/kg-day, and included dilation of the renal pelvis, calculus, and “oxalate crystal nephropathy”. There were significant decreases in body weights among parental females in the mid- and high-dose groups (300 and 600 mg/kg-day, respectively) during gestation, and in high-dose females on day 0 of lactation. There were no differences in body weight gain during gestation and lactation, or in food consumption or food efficiency during gestation. The overall decrease in body weight without a concomitant decrease in body weight gain during the reproductive toxicity portion of the study *possibly* suggests that females had lower body weights (see summary of repeated-dose toxicity) prior to the reproduction phase of the study and that exposures had stopped at day 90.

LOAEL (parental toxicity/males) = 600 mg/kg-day (based on kidney effects)

NOAEL (parental toxicity/males) = 300 mg/kg-day

LOAEL (parental toxicity/females) = 300 mg/kg-day (based on decreases in body weight)

NOAEL (parental toxicity/females) = 150 mg/kg-day

NOAEL (reproductive/developmental toxicity) = 600 mg/kg-day (based on no treatment-related effects observed at the highest dose tested).

Developmental Toxicity

Pregnant Sprague-Dawley rats (25/dose) were administered 0, 75, 150, 300 or 600 mg/kg-day of the test substance in water by oral gavage on days 7 through 21 of gestation. Outcomes assessed included maternal body weight, food consumption, clinical signs and survival; numbers of corpora lutea, live and dead fetuses and resorptions; fetal weight, sex and malformations and variations. There were no maternal mortalities at any dose level. Pregnancy ratios in the 0, 75, 150, 300 or 600 mg/kg-day groups were 25/25, 25/25, 24/25, 23/25 and 23/25, respectively. There was no evidence of maternal or developmental toxicity at 75 or 150 mg/kg-day. At 300 mg/kg-day, lung noise was observed in 2/25 dams and developmental toxicity consisted of a slight, not statistically significant, increase in the incidence of skeletal malformations. At 600 mg/kg/day, maternal effects included significant reductions in body weight and food consumption and significant adverse clinical observations (abnormal gait/staggering, lung noise, irregular respiration and lethargy). There were no remarkable findings post mortem in dams. Developmental toxicity was observed in the 600 mg/kg-day group and consisted of decreased mean fetal weight, increased incidence of fetal malformations (fused and absent ribs, fused and hemivertebra and abnormally fused and cleft/non-fused sternebra) and increased fetal variations (misaligned and incompletely ossified sternebra and incompletely ossified vertebra).

LOAEL (maternal toxicity) = 300 mg/kg-day (based on decreases in body weight and increased clinical signs)

LOAEL (developmental toxicity) = 300 mg/kg-day (based on decreased fetal weight and increased incidence of skeletal malformations and variations)

NOAEL (developmental and maternal toxicity) = 150 mg/kg-day

Genetic Toxicity – Gene Mutation

In vitro

(1) *Salmonella typhimurium* strains TA97a, TA98, TA100 and TA1535 and *Escherichia coli* WP2 *uvrA* (pKM101) were exposed to concentrations of 1, 5, 10, 50, 100, 500, 1000, 2500 or 5000 µg/plate (TA 100 & *E. coli*) or 10, 50, 100, 500, 1000, 2500 or 5000 µg/plate (TA97a, TA98, & TA1535) in the presence and absence of metabolic activation. Positive and solvent controls were tested concurrently, but results of control response were not provided. Two independent trials were conducted. Cytotoxicity was observed at 1000 µg/plate and above.

Glycolic acid was not mutagenic in this assay.

(2) Glycolic acid was also tested by the National Toxicology Program (NTP) and was found to be negative for induction of genetic mutations in bacterial cells (see http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=salmonella.salmonellaData&study_no=A20835&cas_no=79%2D14%2D1&endpointlist=SA)

(3) Mouse lymphoma cells (L5178Y; TK locus) were exposed to concentrations of 39.3, 78.5, 157, 313, 625, 1250, 2500 or 5000 µg/mL in an initial assay and 250, 500, 1000, 2000, 2500, 3000, 4000 or 5000 µg/mL in a confirmatory assay. Both assays were conducted in the presence and absence of metabolic activation. Positive and negative controls were tested concurrently and responded appropriately. No increases in mutations were observed in the absence of metabolic activation. In the presence of metabolic activation, increases in mutant frequency were observed at 2500 µg/ml and above.

Glycolic acid was mutagenic with metabolic activation and not mutagenic without metabolic activation in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vivo

Crl:CD-1 (ICR)BR mice were administered a single oral dose (via gavage) of 300, 600 or 1200 mg/kg-bw (males) or 400, 800 or 1600 mg/kg-bw (females). Five animals per sex were used for the low and mid doses, 10 animals per sex for controls and 15 males and 13 females for the high dose. Positive and negative controls were tested concurrently and responded appropriately. Five males and 3 females from the high-dose group were found dead 1 or 2 days post-dosing. No statistically significant increases in micronuclei were observed in any test substance-treatment group at either 24 or 48 hours.

Glycolic acid did not induce micronuclei in this assay.

Additional Information

Glycolic acid is a strong acid and, at high concentration in solution (~70%) is expected to cause severe skin and eye irritation/corrosion.

Skin Irritation

One male albino rabbit was dosed with 0.5 mL of undiluted glycolic acid (70% technical grade) to intact and abraded skin. The site was covered with gauze and wrapped for 24 hours. Observations were made at 24, 48 and 72 hours after application. Strong erythema and mild edema were noted on the intact skin and strong erythema and necrosis along the lines of abrasion were noted at 24 hours. All erythema was cleared by 72 hours, however, necrosis along the lines of abrasion remained. The robust summary concluded that glycolic acid was a strong irritant bordering on corrosive.

CASRN 79-14-1 was severely irritating to rabbit skin,

Eye Irritation

Two albino rabbits were administered 0.1 mL of undiluted glycolic acid (64% purity) to the right conjunctival sac. After 20 seconds, one treated eye was washed with tap water for 1 minute. The other treated eye was not washed. Observations were made at 1 and 4 hours and at 1, 2, 3, 7 and 14 days. Fluor-I-strip stain and a biomicroscope were used at examination after the day of treatment. Ocular effects in both the washed and unwashed eyes were severe and irreversible. By 14 days, observation was terminated because the treated, unwashed eye had become very small and had no reaction to light. The washed eye reacted to light, although, the cornea appeared as if it would rupture.

CASRN 79-14-1 was severely irritating to rabbit eyes.

Sensitization

In a modified Buehler sensitization study, Hartley guinea pigs (20 animals) were induced with glycolic acid as a 26% w/v solution in normal saline solution. A 0.5 mL aliquot of the solution was applied to clipped, intact skin of the left flank, occluded for 6 hours and then rinsed. Induction sites were scored for irritation approximately 24 and 48 hours following application. This procedure was repeated at 7-day intervals for 3 consecutive weeks. A control group of 10 guinea pigs were treated with saline solution alone. A positive control was not conducted concurrently. Following the third application, the animals were rested for approximately 15 days. On day 29, in the challenge portion of the study, 0.5 mL of a 20% w/v solution in normal saline was applied to the clipped, intact skin of the right flank, occluded for 6 hours and rinsed. Approximately 24 and 48 hours after the challenge application, test sites were examined for dermal irritation or signs of elicited sensitization. The incidence of dermal sensitization was 0/20 (0%).

CASRN was not a skin sensitized in this assay.

Immunotoxicity

In the oral gavage repeated-dose toxicity study described previously, humoral immune responses were evaluated. Briefly, on day 23 of the 90-day study, 10 animals/sex/group were injected with sheep red blood cells (SRBCs). Six days later these animals were sacrificed and their spleen and thymus were removed and weighed. Serum was also collected from each rat and was analyzed for SRBC-specific antibody. A positive control group was also evaluated (using SRBC injection following exposure to cyclophosphamide). The robust summary reported that no treatment-related effects on the humoral immune response were observed (no details were provided).

Neurotoxicity

In the oral gavage repeated-dose toxicity study described previously, neurobehavioral responses were evaluated. Outcomes assessed included a functional observational battery (FOB) and motor activity evaluations; these were performed prior to exposure, and at 3 times during the exposure. Microscopic examinations of brain, spinal cord and skeletal muscle were performed in control and high dose group at the conclusion of the exposure. No treatment-related changes in the FOB or histopathology of the brain, spinal cord, or skeletal muscle were observed. In the developmental toxicity study described above, abnormal gait/staggering was observed in rats that received oral gavage doses of 600 mg/kg-day on days 7-21 of gestation.

Conclusion: The acute toxicity of CASRN 79-14-1 in rats is low by the oral route and moderate by the inhalation route. A 90-day oral gavage repeated-dose toxicity study in rats showed kidney effects (histopathology) and changes in hematology and clinical chemistry changes in males at 300 mg/kg-day and higher; the NOAEL for systemic toxicity is 150 mg/kg-day. A 14-day inhalation repeated-dose toxicity study in rats showed extreme morbidity, decreased body weight, alterations in clinical chemistry and urinalysis parameters, and effects on the thymus, liver, spleen and kidney at 0.51 mg/L/day; the NOAEC for systemic toxicity is 0.16 mg/L/day. In the reproductive toxicity subset of the 90-day oral repeated-dose toxicity study, kidney effects were reported in males at 600 mg/kg-day and decreases in body weight were reported in females at 300 mg/kg-day; the NOAEL for systemic toxicity in males and females is 300 and 150 mg/kg-day, respectively. No treatment-related effects were observed on any of the reproductive parameters measured; the NOAEL for reproductive toxicity is 600 mg/kg-day, the highest dose tested. In an oral prenatal developmental toxicity study with CASRN 79-14-1 in rats, maternal effects included significant reductions in body weight and food consumption, abnormal gait/staggering, lung noise, irregular respiration and lethargy at 300 mg/kg-day; the NOAEL for maternal toxicity is 150 mg/kg-day. Malformations and variations were observed in the fetuses at 300 mg/kg-day; the NOAEL for developmental is 150 mg/kg-day. CASRN 79-14-1 was not mutagenic to bacterial cells, but was mutagenic in mammalian cells *in-vitro*. CASRN 79-14-1 did not induce formation of micronuclei in mice *in-vivo*. CASRN 79-14-1 was irritating to rabbit skin and eyes but did not cause skin sensitization in guinea pigs.

Table 3. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program-Human Health Data	
Endpoints	SPONSORED CHEMICAL Glycolic Acid (79-14-1)
Summary of Human Health Data	
Acute Oral Toxicity LD₅₀ (mg/kg-bw)	LD₅₀ = 1938
Acute Inhalation Toxicity LC₅₀ (mg/L)	LC₅₀ (male) = 3.6 LC₅₀ (female) = 5.2
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-day)	90-Days LOAEL = 300 NOAEL = 150
Repeated-Dose Toxicity NOAEL/LOAEL Inhalation (mg/L/day)	Two-Weeks LOAEL = 0.51 NOAEL = 0.16
Reproductive Toxicity NOAEL Oral (mg/kg-day)	NOAEL = 600 LOAEL/NOAEL (male) = 600/300 LOAEL/NOAEL (female) = 300/150
Reproductive Toxicity	
Parental/Systemic Toxicity	
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-day)	LOAEL = 300 NOAEL = 150 LOAEL = 300 NOAEL = 150
Maternal Toxicity	
Developmental Toxicity	
Genetic Toxicity – Gene Mutation <i>In vitro</i> (Bacterial cells) <i>In vitro</i> (Mammalian cells)	Negative Negative (without activation), Positive (with activation)
Genetic Toxicity – Chromosomal Aberrations <i>In vivo</i>	Negative
Additional Information Skin Irritation Eye Irritation Skin Sensitization Immunotoxicity Neurotoxicity	Highly Irritating Highly Irritating Negative Negative Negative

Bold = measured data.

4. Hazard to the Environment

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 4.

Acute Toxicity to Fish

Fathead minnows (*Pimephales promelas*; 10/concentration) were exposed to CASRN 79-14-1 at nominal concentrations of 0.0064, 0.0081, 0.010, 0.013, 0.016 or 0.020% (v/v) for 96 hours under static conditions. All deaths occurred within 24 hours.

96-h LC₅₀ = 164 mg/L

Acute Toxicity to Aquatic Invertebrates

Water fleas (*Daphnia magna*; 5/replicate, 4 replicates/concentration) were exposed to CASRN 79-14-1 at nominal concentrations of 0, 25, 50, 100, 200, 400 or 800 mg/L for 48 hours under static conditions. There were no sublethal effects observed in the surviving daphnids.

48-h EC₅₀ = 141 mg/L

Toxicity to Aquatic Plants

Green Algae (*Pseudokirchneriella subcapitata*; 3 replicates/concentration) were exposed to CASRN 79-14-1 at mean measured concentrations of 7.52, 14.5, 30.3, 54.6 and 73.6 mg/L for 72 hours. At the end of the 72-hour exposure period, a control replicate and samples from the test concentrations exhibiting a 50% or greater inhibition of cell counts were selected for a recovery test and exposed to nutrient medium for an additional 144 hours. The effects upon growth rate and biomass were found to be algistatic.

72-h EC₅₀ (growth) = 44.0 mg/L

72-h EC₅₀ (biomass) = 21.6 mg/L

Conclusion: For CASRN 79-14-1, the 96-hour LC₅₀ for fish is 164 mg/L (nominal). The 48-hour EC₅₀ for aquatic invertebrates is 141 mg/L (nominal). The 72-hour EC₅₀ for aquatic plants is 44 mg/L (measured) for growth and 21.6 mg/L (measured) for biomass.

Table 4. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Aquatic Toxicity Data	
Endpoints	Glycolic Acid (CASRN 79-14-1)
Fish 96-h LC₅₀ (mg/L)	164*
Aquatic Invertebrates 48-h EC₅₀ (mg/L)	141*
Aquatic Plants 72-h EC₅₀ (mg/L) (growth/biomass)	44/21.6

Bold = measured data; *Nominal concentrations