

**SCREENING-LEVEL HAZARD CHARACTERIZATION
OF HIGH PRODUCTION VOLUME CHEMICALS**

SPONSORED CHEMICAL

**Carbonic Acid, Oxydiethylene Diallyl Ester (CAS No. 142-22-3)
[9th CI Name: 2,5,8,10-Tetraoxatridec-12-enoic Acid, 9-oxo-, 2-propenyl Ester]**

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INTERIM**

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SCREENING-LEVEL HAZARD CHARACTERIZATION OF HIGH PRODUCTION VOLUME CHEMICALS

The High Production Volume (HPV) Challenge Program¹ is 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 sponsor chemicals; sponsorship entails the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data do 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. OPPT is using a hazard-based screening process to prioritize review of the submissions. The hazard-based screening process consists of two tiers described below briefly and in more detail on the Hazard Characterization website³.

Tier 1 is a computerized sorting process whereby key elements of a submitted data set are compared to established criteria to “bin” chemicals/categories for OPPT review. This is an automated process performed on the data as submitted by the sponsor. It does not include evaluation of the quality or completeness of the data.

In Tier 2, a screening-level hazard characterization is developed by EPA that consists of an objective evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. The evaluation is performed according to established EPA guidance^{2,4} and is based primarily on hazard data provided by sponsors. EPA may also include additional or updated hazard information of which EPA, sponsors or other parties have become aware. The hazard characterization may also identify data gaps that will become the basis for a subsequent data needs assessment where deemed necessary. Under the HPV Challenge Program, chemicals that have similar chemical structures, properties and biological activities may be grouped together and their data shared across the resulting category. This approach often significantly reduces the need for conducting tests for all endpoints for all category members. As part of Tier 2, evaluation of chemical category rationale and composition and data extrapolation(s) among category members is performed in accord with established EPA² and OECD⁵ guidance.

The screening-level hazard characterizations that emerge from Tier 2 are important contributors to OPPT’s existing chemicals review process. These hazard characterizations are technical documents intended to support 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. The public, including sponsors, may offer comments on the hazard characterization documents.

The screening-level hazard characterizations, as the name indicates, do not evaluate the potential risks of a chemical or a chemical category, but will serve as a starting point for such reviews. In 2007, EPA received data on uses of and exposures to high-volume TSCA existing chemicals, submitted in accordance with the requirements of the Inventory Update Reporting (IUR) rule. For the chemicals in the HPV Challenge Program, EPA will review the IUR data to evaluate exposure potential. The resulting exposure information will then be combined with the screening-level hazard characterizations to develop screening-level risk characterizations^{4,6}. The screening-level risk characterizations will inform EPA on the need for further work on individual chemicals or categories. Efforts are currently underway to consider how best to utilize these screening-level risk characterizations as part of a risk-based decision-making process on HPV chemicals which applies the results of the successful U.S. High Production Volume Challenge Program and the IUR to support judgments concerning the need, if any, for further action.

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. HPV Chemicals Hazard Characterization website (<http://www.epa.gov/hpvis/abouthc.html>).

⁴ U.S. EPA. Risk Assessment Guidelines; <http://cfpub.epa.gov/ncea/raf/rafguid.cfm>.

⁵ OECD. Guidance on the Development and Use of Chemical Categories; <http://www.oecd.org/dataoecd/60/47/1947509.pdf>.

⁶ U.S. EPA. Risk Characterization Program; <http://www.epa.gov/osa/spc/2riskchr.htm>.

SCREENING-LEVEL HAZARD CHARACTERIZATION

Carbonic acid, oxydiethylene diallyl ester (CAS No. 142-22-3)

Introduction

The sponsor, Great Lakes Chemical Corporation and PPG Industries, Inc., submitted a Test Plan and Robust Summaries to EPA for Carbonic acid, oxydiethylene diallyl ester (CAS No. 142-22-3; 9th CI name: 2,5,8,10-tetraoxatridec-12-enoic acid, 9-oxo-, 2-propenyl ester) on December 18, 2001. EPA posted the submission on the ChemRTK HPV Challenge website on January 15, 2002 (<http://www.epa.gov/hpv/pubs/summaries/craxydler/c13381tc.htm>). EPA comments on the original submission were posted to the website on June 14, 2002. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on June 28, 2002 and February 2, 2006, which were posted to the ChemRTK website on August 7, 2002 and April 14, 2006, respectively.

This screening level hazard characterization is based primarily on the review of the test plan and robust summaries of studies submitted by the sponsor(s) under the HPV Challenge Program. 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. A summary table of SIDS endpoint data with the structure(s) of the sponsored chemical(s) is included in the appendix. The screening-level hazard characterization for environmental and human health effects is based largely on SIDS endpoints and is described according to established EPA or OECD effect level definitions and hazard assessment practices.

Summary-Conclusion

The log K_{ow} of carbonic acid, oxydiethylene diallyl ester indicates that its potential to bioaccumulate is expected to be low. Carbonic acid, oxydiethylene diallyl ester is readily biodegradable, indicating that it is not expected to persist in the environment.

The evaluation of available toxicity data indicates that the potential acute hazard of carbonic acid, oxydiethylene diallyl ester to fish is high, to aquatic invertebrates is low and to aquatic plants is moderate.

Acute oral toxicity of carbonic acid, oxydiethylene diallyl ester to rats is moderate and acute dermal toxicity to rabbits is low. Carbonic acid, oxydiethylene diallyl ester is highly irritating to rabbit skin, slightly irritating to rabbit eyes and is not a dermal sensitizer in guinea pigs or rabbits. Repeated dermal exposure of rats to the chemical showed no systemic toxicity, neurobehavioral changes or reproductive toxicity or any developmental effects in the offspring. However, at extremely high doses, dermal toxicity was associated with mortality, decreased food consumption and emaciation and decreased food and water consumption, body weight and spleen and heart weight and increased brain-to-body weight. Following repeated dermal exposures of pregnant rabbits during days 6 – 18 of gestation, signs of maternal toxicity included mortality, decreased body weight and liver, heart, kidney and mesentary changes. Developmental toxicity included high incidence of resorptions in animals dying, aborting and early littering, increased incidence of ocular abnormalities and a decrease in incidence of single thirteenth ribs. Carbonic acid, oxydiethylene diallyl ester was mutagenic in a bacteria, but did not induce chromosomal aberrations or unscheduled DNA synthesis in mammalian cells.

The potential health hazard of carbonic acid, oxydiethylene diallyl ester is low. Available data suggest that carbonic acid, oxydiethylene diallyl ester has the potential to be genotoxic.

No data gaps were identified under the HPV Challenge Program.

1. Physical-Chemical Properties and Environmental Fate

A summary of physical-chemical and environmental fate data submitted is provided in the Appendix. For the purpose of the screening-level hazard characterization, the review and summary of these data were limited to the octanol-water partition coefficient and biodegradation endpoints as indicators of bioaccumulation and persistence, respectively.

Octanol-Water Partition Coefficient

Log K_{ow} : 1.54 (estimated)

Biodegradation

In the Closed Bottle method using activated domestic sludge as inoculum, 73.2% of carbonic acid, oxydiethylene diallyl ester had degraded after 28 days.

Carbonic acid, oxydiethylene diallyl ester is readily biodegradable.

Conclusion: The log K_{ow} of carbonic acid, oxydiethylene diallyl ester indicates that its potential to bioaccumulate is expected to be low. Carbonic acid, oxydiethylene diallyl ester is readily biodegradable, indicating that it does not have potential to persist in the environment.

2. Environmental Effects – Aquatic Toxicity

Acute Toxicity to Fish

Bluegill sunfish (*Lepomis macrochirus*) were exposed to carbonic acid, oxydiethylene diallyl ester at nominal concentrations of 0, 0.22, 0.36, 0.60, 1.0 or 1.7 mg/L under static conditions for 96 hours. All fish exposed to 1.7 mg/L died within 24 hours and all fish exposed to 1.0 mg/L died within 48 hours. Mortality rates at 96 hours were 40, 10, 0 and 0% for the 0.60, 0.36 and 0.22 mg/L and control, respectively.

96-h LC₅₀ = 0.57 mg/L

Acute Toxicity to Aquatic Invertebrates

Daphnia magna were exposed to carbonic acid, oxydiethylene diallyl ester at nominal concentrations of 0, 6.4, 11, 18, 30 or 50 mg/L under static conditions for 48 hours. In the 30 and 50 mg/L concentrations, complete lethality was observed by 24 hours. At 18 mg/L, mortality rates were 20, 0 and 80% for the three replicates and no discernible effect was noted at 11 mg/L or below.

48-h EC₅₀ = 18 mg/L

Toxicity to Aquatic Plants

(1) *Pseudokirchneriella subcapitata* were exposed to carbonic acid, oxydiethylene diallyl ester at nominal concentrations of 0.625, 1.25, 2.5, 5.0 and 10 mg/L under static conditions for 96 hours. Test concentrations were achieved using triethylene glycol as a solvent. Precipitation was noted at concentrations >10mg/L. Chlorophyll fluorescence (biomass) with respect to the solvent control was increased (35%) at 2.5 mg/L. All other treatments induced anywhere from a 12% decrease (0.625 mg/L) to a 9% increase (1.25 mg/L). There was no concentration-dependent effect of test material on algae biomass.

NOEC > 10 mg/L (biomass)

(2) *Skeletonema costatum* were exposed to carbonic acid, oxydiethylene diallyl ester at nominal concentrations of 0.357, 0.714, 1.43, 2.86, 5.72 and 11.43 mg/L under static conditions for 96 hours. Test concentrations were achieved using triethylene glycol as a solvent. Precipitation was noted at concentrations >10mg/L. Chlorophyll fluorescence (biomass) with respect to the solvent control was increased (9%) at 1.43 mg/L. All other treatments induced decreases of 21, 9 and 5% at concentrations of 2.86, 5.72 and 11.43 mg/L. Compared to solvent control a

decrease in growth (15 and 7%) was reported at 5.72 and 11.43 mg/L, respectively. There was no concentration-dependent effect of test material on algae growth or biomass.

NOEC > 10 mg/L (growth and biomass)

In comments on the original test plan, EPA noted the use of triethylene glycol as a solvent and asked the sponsor to provide a rationale for the use of solvent. No rationale was provided. Based on in-depth review of the study summary, EPA agrees with the general conclusions of the sponsor, that no effects were observed up to the apparent solubility limit of the test substance in algal growth media (10 mg/L). Based on this concentration, EPA would characterize the hazard to plants as low. However, due to uncertainties regarding the rationale and potential effects of the solvent on the test, EPA estimated plant toxicity using ECOSAR, which provides an 96-h LC₅₀ of 5.7 mg/L, which indicates the hazard to plants as moderate. Given uncertainties regarding the submitted test data, EPA concludes the potential hazard of oxydiethylene diallyl ester to plants is moderate.

Conclusion: The evaluation of available toxicity data indicates that the potential acute hazard of carbonic acid, oxydiethylene diallyl ester to fish is high, to aquatic invertebrates is low and to aquatic plants is moderate.

3. Human Health Effects

Acute Oral Toxicity

(1) Fischer 344 rats (5/sex/dose) were administered the test substance via gavage at 100, 400, 600 or 800 mg/kg-bw in corn oil and observed for up to 14 days. Mortalities occurred at 400, 600 and 800 mg/kg-bw.

LD₅₀ = 515 mg/kg-bw

(2) Charles River rats (2/sex/dose) were administered the test substance via gavage at 177.8, 266.7, 400, 600 or 900 mg/kg-bw in corn oil and observed for 14 days. Mortality occurred at 266.7 mg/kg-bw and higher. All deaths occurred within 3 days of dose administration. All animals that died exhibited pale livers and hemorrhage in the gastrointestinal tract. No gross observations were noted in survivors.

LD₅₀ = 349 mg/kg-bw

Acute Dermal Toxicity

(1) New Zealand White rabbits (4/sex) were administered the test substance via dermal route at 10 mL/kg-bw (approximately 11,430 mg/kg-bw) to clipped, intact skin under occluded conditions for 24 hours and were observed for 4 days following the exposure period. Mortality was seen at this dose. Signs of hemorrhage were observed in animals that died. Two survivors had irregular, pale foci on the liver. Slight to moderate erythema and edema were noted during days 1 – 3.

LD₅₀ ~ 11,430 mg/kg-bw

(2) New Zealand White rabbits (2 males and 4 females) were administered the test substance via dermal route at 5 mL/kg-bw (approximately 5715 mg/kg-bw) to abraded skin under occluded conditions for 24 hours and were observed for 13 days. No deaths occurred. One animal had diffuse intermingled pale white to yellow foci on the liver upon necropsy. Slight to moderate erythema and edema, slight eschar formation, scaling and cracking were noted.

LD₅₀ ~ 5715 mg/kg-bw

(3) New Zealand White rabbits (4/dose) were administered the test substance via dermal route at 3038 or 10,250 mg/kg-bw to shaved, intact skin under occluded conditions for 24 hours and were observed for 14 days following exposure. Mortality was seen at both doses. Skin irritation characterized by red, well-defined erythema and severe edema was seen at the applications sites at 24 hours after dose administration. Dryness was evident after 14 days. No other skin alterations were noted.

LD₅₀ = 3038 – 10,250 mg/kg-bw

Repeated-Dose Toxicity

(1) In a combined repeated-dose/reproductive/developmental toxicity study, Sprague-Dawley rats (10/sex/dose) were administered the test substance via dermal route at 0, 150, 454 or 1030 mg/kg-bw/day for 6 hours/day under occluded conditions, for 42 days (14 days pre-mating, 14 days during mating and 14 days post-mating). Neurobehavioral evaluations for motor activity, auditory response, grip strength and pupillary and corneal reflexes were conducted before the test and just prior to terminal sacrifice after 42 days of exposure. Organs and tissues from control and high-dose rats were preserved and examined microscopically. In addition, nervous system tissues from control, mid- and high-dose females were examined with special neuropathology staining. No effects of treatment were observed on mortality; body or organ weights; food consumption or in clinical, neurobehavioral, dermal, hematological, serum chemistry, macroscopic or microscopic evaluations.

LOAEL > 1030 mg/kg-bw/day

NOAEL = 1030 mg/kg-bw/day (based on no effects at the highest dose tested)

(2) CD Charles River rats (5/sex/dose) were administered the test substance via dermal route at 0, 0.08, 0.4 or 2 mL/kg-bw/day (approximately 0, 91, 457 or 2286 mg/kg-bw/day, respectively, based on density) for 14 days. No signs of toxicity or skin irritation were observed in any rats treated with 91 and 457 mg/kg-bw/day. After the second day of application, most of the high-dose animals had an accumulation of red material around the eyes, nose and mouth. Test material also appeared to be accumulating at the shaved hairline. After the fifth day of application, food consumption and defecation was reduced in all high-dose animals. Urinalysis of the four male rats revealed increased ketone and protein concentrations. One high-dose male died on day 8. Necropsy revealed extreme emaciation (total lack of fat tissue) and red, caked material around the eyes and external nares and emaciation. The bladder was filled with coffee-colored liquid; the mucosa of the hind-stomach was hyperemic.

LOAEL ~ 2286 mg/kg-bw/day (based on mortality, decreased food consumption, emaciation)

NOAEL ~ 457 mg/kg-bw/day

(3) CD Charles River rats (5/sex) were administered the test substance via dermal route to shaved skin at 2 mL/kg-bw (approximately 4572 mg/kg-bw/day) twice daily for 14 days. Mean body weights for treated males were significantly less than controls. Food consumption for treated males and water consumption for treated females were lower than controls. There was no effect of treatment on urinalysis or serum chemistries. Brownish coloration of the shaved hair area, red encrustation around the eyelids and the general absence of fatty tissues were noted in 4/5 of treated rats at necropsy. Spleen and heart weights in treated males were lower and brain/body weight ratios were higher than those of controls.

LOAEL ~ 4572 mg/kg-bw/day (based on decreased body weight, food consumption and water consumption, decreased spleen and heart weights and increased brain to body weight ratio)

NOAEL = Not established

Reproductive/Developmental Toxicity

(1) In the combined repeated-dose/reproductive/developmental toxicity study described previously, no treatment-related effects were evident for reproductive performance (male and female fertility and mating indices), gestation and lactation body weights or food consumption, gestation lengths or litter size to postnatal day (PND) 4. No treatment-related effects were evident for gestation length, litter size, pup body weight, pup sex ratios, pup survival or pup external examinations to PND 4.

NOAEL (systemic and reproductive/developmental toxicity) = 1030 mg/kg-bw/day (based on no effects at the highest dose tested)

(2) Pregnant New Zealand White rabbits (18/dose) were administered the test substance via dermal route at 0, 0.1, 0.5 or 1.0 mL/kg-bw/day (approximately 0, 114.3, 571.5 or 1143 mg/kg-bw/day, respectively) under non-occluded conditions for 6 hours/day during gestation days 6 to 18. Six rabbits at the high-dose level died and one was sacrificed. Two, zero, three and eight rabbits treated with control, low-, mid- or high-dose, respectively, were sacrificed before study termination due to abortion or early littering. Skin lesions were present in some animals from all treatment groups. All high-dose rabbits lost weight throughout the study and mid-dose animals lost weight during the gestation days 6 – 18. Pale foci, firmness and/or irregular surface of the liver were common findings in the high-dose animals and one mid-dose animal. Other findings included pale foci or pale areas on the heart, kidneys and/or mesentery. In the high-dose group, there was a high incidence of resorptions in animals dying, aborting, littering early or sacrificed preterm. The ovarian and uterine endpoints for low- and mid-dose animals were similar to controls. The incidence of major malformations, minor skeletal variations and visceral anomalies in

the litters of treated females were similar to controls. At the mid- and high-dose, the incidence of small or oval lenses was slightly higher than control. One of the affected fetuses at the high dose and three at the middle dose also had ocular opacities. Other ocular findings (lenses formed in two layers) were also noted in three fetuses at the middle dose and one at the high dose. At the middle dose, there was a significant decrease in the incidence of single thirteenth ribs and accompanying increases in the incidence of paired thirteenth ribs and 27 pre-sacral vertebrae.

LOAEL (maternal toxicity) ~ 571 mg/kg-bw/day (based on mortality, decreased body weight, liver changes)

NOAEL (maternal toxicity) ~ 114 mg/kg-bw/day

LOAEL (developmental toxicity) ~ 571 mg/kg-bw/day (based on abortion, early littering, increased incidence of ocular abnormalities, decrease in incidence of thirteenth ribs)

NOAEL (developmental toxicity) ~ 114 mg/kg-bw/day

Genetic Toxicity – Gene Mutation

In vitro

Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to the test substance at concentrations of 0, 0.003, 0.01, 0.03, 0.1, 0.3, 1, 3 and 10% in the presence and absence of metabolic activation. The cytotoxic concentration was 10%. In the presence of metabolic activation, concentrations of 0.003, 0.01 and 0.03% caused dose-dependent increases in revertants that were at least 3 times greater than that of control. The positive controls responded appropriately.

Carbonic acid, oxydiethylene diallyl ester was mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vitro

Human peripheral blood lymphocytes were exposed to the test substance at concentrations ranging from 313 – 5000 µg/mL in the absence of metabolic activation for 4 and 20 hours and to concentrations ranging from 125 – 1250 µg/mL in the presence of metabolic activation for 4 hours. The cytotoxic concentration was ≥ 5000 µg/mL in the absence of metabolic activation and ≥ 1250 µg/mL in the presence of metabolic activation. Positive control testing and response was not mentioned in the robust summary.

Carbonic acid, oxydiethylene diallyl ester did not induce chromosomal aberrations in this assay.

Genetic Toxicity – Other

In vitro

In an unscheduled DNA synthesis assay, primary rat hepatocytes were exposed to the test substance at concentrations of 0.3313 – 10 nL/mL without metabolic activation for 1 hour and then washed. The cytotoxic concentration was 2.5 nL/mL. Positive controls were tested concurrently and responded appropriately.

Carbonic acid, oxydiethylene diallyl ester did not induce unscheduled DNA synthesis in this assay.

Additional Information

Skin Irritation

(1) Undiluted test material (0.5 mL) was applied to one intact and one abraded skin site on rabbits (3/sex) under occluded conditions for 6 hours and assessed for up to 13 days after exposure. At 48 hours, moderate to severe erythema were noted on all sites and by 72 hours, irritation progressed to necrosis with severe erythema and very slight edema. Reddened and blackened skin at all sites was noted. By 13 days, edema, but not erythema, resolved.

Carbonic acid, oxydiethylene diallyl ester was slightly to highly irritating to rabbit skin.

(2) Undiluted test material (0.5 mL) was applied to one intact and one abraded skin site on four rabbits under occluded conditions for 24 hours and assessed for up to 72 hours after exposure. In three of the four rabbits, both abraded and non-abraded sites showed severe erythema and edema at 24 and 72 hours.

Carbonic acid, oxydiethylene diallyl ester was highly irritating to rabbit skin.

(3) New Zealand White rabbits (females, number per group not reported) were administered the test substance via dermal route (0.5 mL of undiluted) to intact and abraded skin under occluded conditions for 24 hours and assessed

for up to 72 hours after exposure. Application of test substance produced slight erythema in some animals at 24 hours. Total recovery was achieved by day 8. The test substance was slightly irritating to rabbit skin in this assay. **Carbonic acid, oxydiethylene diallyl ester was slightly irritating to rabbit skin.**

Eye Irritation

Undiluted test material (0.1 mL) was instilled in the conjunctival sac of the right eye of five rabbits. Test eyes were not washed. Irritation was scored at 1 minute, 1, 24 and 72 hours and 7 days after administration. Conjunctival redness and slight discharge was seen which was resolved by 24 – 72 hours.

Carbonic acid, oxydiethylene diallyl ester was slightly irritating to rabbit eyes.

Sensitization

(1) Rabbits (3/sex) were dosed with 0.5 mL of undiluted carbonic acid, oxydiethylene diallyl ester applied to one intact and one abraded skin site and 0.5 mL of test material diluted with 0.2 mL of physiological saline was applied to one intact and one abraded skin site under occluded conditions for 6 hours. Twenty-six days after the original application, animals were challenged with 0.5 mL of the test substance for 6 hours. Reactions were scored for up to 72 hours after challenge. A third trial was performed 21 days after the second application with 0.5 mL of the test substance for 6 hours. Reactions were scored for up to 7 days following exposure. The test substance caused sporadic irritation with necrosis. Tissues sent for examination showed no evidence of deposits of IgG in arterial walls. Therefore, irritation was not caused by an IgG-related immune response and the material was not determined to be a sensitizer.

Carbonic acid, oxydiethylene diallyl ester was not a skin sensitizer in rabbit.

(2) Guinea pigs (10/sex) were dosed with 0.4 mL of carbonic acid, oxydiethylene diallyl ester (the same as that used in the rabbit sensitization study above) to shaved intact skin under occluded conditions for 6 hours. Patches were reapplied to the same site of test animals once a week for a total of three applications. After a 2-week rest period, a fresh application site was challenged with 0.4 mL of the test substance as described previously. During the primary challenge, all 20 animals did not show any irritation at the 24- and 48-hour readings.

Carbonic acid, oxydiethylene diallyl ester was not a skin sensitizer in guinea pigs.

Conclusion: Acute oral toxicity of carbonic acid, oxydiethylene diallyl ester to rats is moderate and acute dermal toxicity to rabbits is low. Carbonic acid, oxydiethylene diallyl ester is highly irritating to rabbit skin, slightly irritating to rabbit eyes and is not a dermal sensitizer in guinea pigs or rabbits. Repeated dermal exposure of rats to the chemical showed no systemic toxicity, neurobehavioral changes or reproductive toxicity or any developmental effects in the offspring. However, at extremely high doses, dermal toxicity was associated with mortality, decreased food consumption and emaciation and decreased food and water consumption, body weight and spleen and heart weight and increased brain-to-body weight. Following repeated dermal exposures of pregnant rabbits during days 6 – 18 of gestation, signs of maternal toxicity included mortality, decreased body weight and liver, heart, kidney and mesentary changes. Developmental toxicity included high incidence of resorptions in animals dying, aborting and early littering, increased incidence of ocular abnormalities and a decrease in incidence of single thirteenth ribs. Carbonic acid, oxydiethylene diallyl ester was mutagenic in a bacteria, but did not induce chromosomal aberrations or unscheduled DNA synthesis in mammalian cells.

The potential health hazard of carbonic acid, oxydiethylene diallyl ester is low. Available data suggest that carbonic acid, oxydiethylene diallyl ester has the potential to be genotoxic.

4. Hazard Characterization

The log K_{ow} of carbonic acid, oxydiethylene diallyl ester indicates that its potential to bioaccumulate is expected to be low. Carbonic acid, oxydiethylene diallyl ester is readily biodegradable, indicating that it is not expected to persist in the environment.

The evaluation of available toxicity data indicates that the potential acute hazard of carbonic acid, oxydiethylene diallyl ester to fish is high and to aquatic invertebrates is low.

Acute oral toxicity of carbonic acid, oxydiethylene diallyl ester to rats is moderate and acute dermal toxicity to rabbits is low. Carbonic acid, oxydiethylene diallyl ester is highly irritating to rabbit skin, slightly irritating to rabbit eyes and is not a dermal sensitizer in guinea pigs or rabbits. Repeated dermal exposure of rats to the chemical showed no systemic toxicity, neurobehavioral changes or reproductive toxicity or any developmental effects in the offspring. However, at extremely high doses, dermal toxicity was associated with mortality, decreased food consumption and emaciation and decreased food and water consumption, body weight and spleen and heart weight and increased brain-to-body weight. Following repeated dermal exposures of pregnant rabbits during days 6 – 18 of gestation, signs of maternal toxicity included mortality, decreased body weight and liver, heart, kidney and mesentary changes. Developmental toxicity included high incidence of resorptions in animals dying, aborting and early littering, increased incidence of ocular abnormalities and a decrease in incidence of single thirteenth ribs. Carbonic acid, oxydiethylene diallyl ester was mutagenic in a bacteria, but did not induce chromosomal aberrations or unscheduled DNA synthesis in mammalian cells.

The potential health hazard of carbonic acid, oxydiethylene diallyl ester is low. Available data suggest that carbonic acid, oxydiethylene diallyl ester has the potential to be genotoxic.

5. Data Gaps

No data gape were identified under the HPV Challenge Program.

APPENDIX 1

Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program	
Endpoints	SPONSORED CHEMICAL Carbonic acid, oxydiethylene diallyl ester (142-22-3)
Structure	
Summary of Physical-Chemical Properties and Environmental Fate Data	
Melting Point (°C)	-4 – 0
Boiling Point (°C)	160 (2.67 hPa)
Vapor Pressure (hPa at 25°C)	Inadequate data. Testing was recommended.
Log K_{ow}	1.54
Water Solubility (mg/L at 25°C)	Inadequate data. Testing was recommended.
Direct Photodegradation	–
Indirect (OH⁻) Photodegradation Half-life (t_{1/2})	0.146 days (estimated)
Stability in Water (Hydrolysis) (t_{1/2})	> 1 yr (pH 4); 280 d (pH 7); 68.4 h (pH 9)
Fugacity (Level III Model)	
Air (%)	0.23
Water (%)	46.7
Soil (%)	52.9
Sediment (%)	0.115
Biodegradation at 28 days (%)	73.2 Readily biodegradable
Summary of Environmental Effects – Aquatic Toxicity Data	
Fish 96-h LC₅₀ (mg/L)	0.57
Aquatic Invertebrates 48-h EC₅₀ (mg/L)	18
Aquatic Plants 72-h EC₅₀ (mg/L)	
(growth)	NOEC > 10 5.7 (estimated)
(biomass)	NOEC > 10

Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program	
Endpoints	SPONSORED CHEMICAL Carbonic acid, oxydiethylene diallyl ester (142-22-3)
Summary of Human Health Data	
Acute Oral Toxicity LD ₅₀ (mg/kg-bw)	349 – 515
Acute Dermal Toxicity LD ₅₀ (mg/kg-bw)	3038 – 10,250
Repeated-Dose Toxicity NOAEL/LOAEL Dermal (mg/kg-bw/day)	NOAEL = ~ 457.2 (14-d) LOAEL = ~ 2286 (14-d)
Reproductive/Developmental Toxicity NOAEL/LOAEL Dermal (mg/kg-bw/day) Systemic and Reproductive/Developmental Toxicity	NOAEL = 1030 LOAEL > 1030
Developmental Toxicity NOAEL/LOAEL Dermal (mg/kg-bw/day) Maternal and Developmental Toxicity	NOAEL ~ 114 LOAEL ~ 572
Genetic Toxicity – Gene Mutation <i>In vitro</i>	Positive
Genetic Toxicity – Chromosomal Aberrations <i>In vitro</i>	Negative
Genetic Toxicity – Other <i>In vitro</i> Unscheduled DNA Synthesis	Negative
Additional Information Skin Irritation Eye Irritation Skin Sensitization	Slightly to highly irritating Slightly irritating Not Sensitizing

– indicates that endpoint was not addressed for this chemical.