

201-16192A

TEST PLAN FOR CARBONIC ACID, OXYDIETHYLENE DIALLYL ESTER  
(CAS NO. 142-22-3)

OVERVIEW

Great Lakes Chemical Corporation and PPG Industries, Inc. jointly agree to sponsor CARBONIC ACID, OXYDIETHYLENE DIALLYL ESTER (CAS NO. 142-22-3) under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Chemical Challenge Program. A common synonym for this chemical is diallyl diglycol carbonate (DAC), which is the chemical name that will be utilized throughout this document. The companies hereby submit a test plan for this substance. All Screening Information Set (SIDS) endpoints for environmental fate, ecotoxicity, and human health effects have been fulfilled.

CAS No. 142-22-3	Information Available	Acceptable	New Testing Required
ENDPOINT	Y/N	Y/N	Y/N
Melting Point	Y	Y	N
Boiling Point	Y	Y	N
Density	Y	Y	N
Vapor Pressure	Y	Y	N
Water Solubility	Y	Y	N
Kow	Y	Y	N
<b>ENVIRONMENTAL FATE</b>			
Photodegradation	Y	Y	N
Stability in Water	Y	Y	N
Biodegradation	Y	Y	N
Transport between Environmental Compartments (Fugacity)	Y	Y	N
<b>TOXICITY</b>			
Acute Toxicity to Fish	Y	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	Y	N
Toxicity to Aquatic Plants	Y	Y	N
<b>TOXICITY TO HUMAN HEALTH</b>			
Acute Toxicity	Y	Y	N
Repeated Dose Toxicity	Y	Y	N
Genetic Toxicity-Mutation	Y	Y	N
Genetic Toxicity-Chromosomal Aberrations	Y	Y	N
Toxicity to Reproduction	Y	Y	N
Developmental Toxicity	Y	Y	N

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## 1. Sponsoring Companies

Great Lakes Chemical Company and PPG Industries, Inc. are the United States manufacturers of diallyl diglycol carbonate (DAC) and are the joint sponsors of this substances in the U. S. Environmental Protection Agency's HPV Chemical Challenge Program. The technical contacts at these companies are:

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## 2. Identity of Sponsored Substance

DAC (CAS No. 142-22-3) is a monomer representing a single chemical substance. The commercially available product (and that utilized in testing) is approximately 90% DAC monomer with the remainder of the product containing oligomers of DAC. The oligomers contain 2-5 DAC units. The primary use is as an industrial intermediate which is polymerized into allyl resins to make optical lenses. The molecular structure of DAC monomer is as follows:



DAC is a clear, colorless liquid at room temperature, with a melting point of -4 to 0 degrees C and a boiling point of 160 degrees C at 2.7 hPa.

## 3. Criteria for Determining Adequacy of Data

All relevant studies were reviewed and assessed for adequacy according to the standards of Klimisch et al. (1997). Studies receiving a Klimisch rating of 1 or 2 were considered to be adequate.

## 4. Test Plan

### 4.1 Physical/Chemical Properties

Data are available for melting point, boiling point, density and water solubility; these data were located in the IUCLID data set from the European Chemicals Bureau (2000). Data for vapor pressure and partition coefficient (Kow) are estimated (calculated) using a modeling approach.

Melting point:	-4 to 0 degrees C
Boiling point:	160 degrees C @ 2.7 hPa
Density:	1.14-1.15 g/cm <sup>3</sup> @ 20 degrees C
Water solubility:	< 0.1 g/l @ 20 degrees C
Vapor pressure:	0.00146 hPa @ 25 degrees C
Log Pow:	1.543

## 4.2 Environmental Fate/Pathways

Results of an OECD guideline study indicate that DAC is readily biodegradable. Data for photodegradation and environmental transport are estimated (calculated) using the EPIWIN/AOP Program. The photodegradation hydroxyl radical rate constant is estimated to be  $73.2806 \text{ E-}12 \text{ cm}^3/\text{molecule-sec}$  with an atmospheric half-life calculated to be 0.146 days. Mackay Level III Fugacity modeling indicates that DAC should partition primarily to water (46.7%) and soil (52.9%), with smaller percentages in air (0.23%) and sediment (0.115%) under hypothetical equilibrium conditions. The hydrolysis half-life of DAC was determined to be 280 days at pH 7 and 25°C (Mullee, 2005). At pH 4 and 25°C, the hydrolysis half-life was calculated to be greater than 1 year and at pH 9 and 25°C, it was determined to be 68 hours.

## 4.3 Ecotoxicity

### 4.3.1 Acute Toxicity to Fish

This endpoint is filled from data from two adequate fish toxicity tests (Sousa, 1982; Ward, 1982b). The LC<sub>50</sub> values for DAC in freshwater and saltwater species are 0.57 mg/l and 0.707 mg/l, respectively.

### 4.3.2 Acute Toxicity to Aquatic Invertebrates

This endpoint is filled from data from one study in *Daphnia magna* (Suprenant et al., 1982) and another in *Mysidopsis bahia* (mysid shrimp) (Ward, 1982a). The 48-hour EC<sub>50</sub> values for DAC in these species are 18 mg/l and 70.7 mg/l, respectively.

### 4.3.3 Acute Toxicity to Aquatic Plants

This endpoint is filled from data from one study in *Selenastrum capricornutum* (freshwater algae) (Maziarz, 1983a) and another in *Skeletonema costatum* (saltwater algae) (Maziarz, 1983b). The no observable effect concentration for DAC in both of these species is 10 mg/l (the highest concentration used in the study).

## 4.4 Human Health Data

### 4.4.1 Acute Mammalian Toxicity

This endpoint is filled by two sufficient oral toxicity studies in rats (Ebbens, 1971; Kingery and Mahew, 1981a) and three dermal toxicity studies in rabbits (Ebbens, 1971; Kingery and Mahew, 1981b,c). The oral LD<sub>50</sub> values for DAC in rats range from 349.5 – 515 mg/kg, and the dermal LD<sub>50</sub> values range from 3038 - 10250 mg/kg.

### 4.4.2 Repeated Dose Mammalian Toxicity

Data from two 14-day dermal toxicity tests in rats were summarized (Lequire et al., 1980; McGahan and Mahew, 1980). Results of the study by McGahan and Mahew (1980) indicate a

NOEL of 0.4 ml/kg/day. A NOEL was not determined in the study by Lequire et al., as effects were noted at the only dose tested.

A repeat dose toxicity study with neurobehavioral evaluations and a reproduction/developmental toxicity screening study was conducted with DAC (Schroeder, 2005). Both the repeat dose and the reproductive/developmental components were comprised of three treatment groups and a saline-treated control group. Each repeat dose group contained ten male and ten female Sprague-Dawley rats. The test article was administered dermally once daily via occlusion for 6 hours. Dose levels were 150, 454, and 1030 mg/kg/day. Males and females in the repeat dose component were treated for at least 42 days. All rats were observed twice daily for morbidity, mortality, and signs of injury. Observations of the animals included clinical signs, neurobehavioral observations, dermal evaluation, body weights, and food consumption. Evaluations for motor activity and emotionality, and other behavioral observations, were conducted pretest, and prior to scheduled terminal euthanasia. Blood collections of clinical pathology evaluations were conducted at study termination. Complete necropsies were performed on all animals; selected organs and tissues were collected, weighed, and preserved. Organs and tissues from control and high-dose animals in the repeat dose component were examined microscopically. In addition, nervous system tissue from female animals from the mid and high repeat dose groups (454 and 1030 mg/kg/day, respectively) as well as from the controls were further processed with special neuropathology staining to allow for better examination of possible nervous system effects. No effect of treatment was evident for mortality, clinical evaluations, neurobehavioral evaluations, dermal evaluations, body weights, food consumption, hematological evaluations, serum clinical chemistry, organ weights, macroscopic, or microscopic evaluations. For systemic toxicity, the No-Observable-Adverse-Effect Level (NOAEL) of DAC was 1030 mg/kg/day, the highest dose level evaluated.

#### **4.4.3 Genetic Toxicity**

##### **4.4.3.1 Mutagenicity**

DAC has been tested for mutagenicity in *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 in the absence and presence of a metabolic activation system (Schechtman et al., 1980) and in an unscheduled DNA synthesis assay in cultured rat hepatocytes (Myhr and Brusick, 1980). Results of both studies were negative (with the exception of a positive result in Salmonella strain TA98). The positive result in strain TA98 is questionable, since it was not dose-dependent and did not occur in other strains with frame-shift mutations (TA1537 and TA1538).

##### **4.4.3.2 Chromosomal aberration**

A chromosome aberration assay was performed and used to evaluate the clastogenic potential of DAC (Gudi and Rao, 2004). DAC was soluble in dimethyl sulfoxide (DMSO), the solvent of choice, at a concentration of 500 mg/ml, the maximum concentration tested for solubility. In the assay, the cells were treated for 4 and 20 hours in the non-activated test system and for 4 hours in the S9 activated test system. All cells were harvested 20 hours after treatment initiation. DAC was soluble in DMSO at all concentrations tested. Visible precipitate was observed in

treatment medium at concentrations greater to or equal to 625 ug/ml at the beginning of the treatment period. Concentrations less than or equal to 500 ug/ml were soluble in treatment medium at the beginning of the treatment period while concentrations less than or equal to 1250 ug/ml were soluble in treatment medium at the end of the treatment period. Visible precipitate was observed in treatment medium at concentrations greater to or equal to 2500 ug/ml at the conclusion of treatment period. Selection of doses for microscopic analysis was based on precipitation of the test article in treatment medium or mitotic inhibition (the lowest dose with at least 50% reduction in mitotic index, relative to the solvent control and two lower doses) in all harvests. The percentage of cells with structural or numerical aberrations in the DAC-treated groups was not significantly increased above that of the solvent control at any dose level. Thus, DAC was concluded to be negative for the induction of structural and numerical chromosome aberrations in the in vitro mammalian chromosome aberration test using human peripheral lymphocytes.

#### **4.4.4 Reproductive Toxicity**

A repeat dose toxicity study with neurobehavioral evaluations (see Section 4.4.2 for details regarding the study protocol) and a reproduction/developmental toxicity screening study was conducted with DAC (MPI, 2005). The purpose of the reproduction/developmental toxicity screening component was to provide information on possible effects on male and female reproductive performance, such as gonadal function, mating behavior, conception, development of the conceptus, and parturition. Males in the repeat dose component were treated for at least 42 consecutive days, while females in the reproductive component were treated for two weeks before pairing, during pairing, and from Gestation Days (GD) 0 to 20. After two weeks of treatment, the females were cohabited nightly with males from the repeat dose component, one male to one female, from the same treatment group, for up to 14 days. Females were evaluated daily for evidence of mating. Once mating was confirmed (GD 0), females were separated from the males for the remainder of gestation, and allowed to deliver and nurse litters until Postnatal Day (PND) 4. Litter size (number of stillborn and live born pups) and pup evaluations (body weight, sexing, and external examination) were recorded at birth and PND 4. Pups were euthanized and externally examined on PND 4 and the carcasses were discarded without further examination. Complete necropsies were performed on all animals; selected organs and tissues were collected, weighed, and preserved. In the reproductive component, no effect of treatment was evident for reproductive performance (male and female fertility and mating indices), gestation and lactation body weights or food consumption, gestation length, or litter size to PND 4. The No-Observable-Effect Level (NOEL) for reproductive performance was 1030 mg/kg/day, the highest dose level evaluated.

#### **4.4.5 Developmental Toxicity**

Data from a teratology study in rabbits shows that DAC is not a developmental toxicant (Robinson et al., 1986). Effects in pups only occurred at doses that caused maternal toxicity. The NOEL for developmental toxicity was 0.1 ml/kg/day.

Developmental effects were also evaluated in a repeat dose toxicity study with neurobehavioral evaluations (see Section 4.4.2 for details regarding the study protocol) and a reproduction/developmental toxicity screening study conducted with DAC (MPI, 2005). The

purpose of the reproductive/developmental toxicity screening component was to provide information on possible effects on male and female reproductive performance, such as gonadal function, mating behavior, conception, the development of the conceptus, and parturition. Males in the repeat dose component were treated for at least 42 consecutive days, while females in the reproductive component were treated for two weeks before pairing, during pairing, and from Gestation Days (GD) 0 to 20. After two weeks of treatment, the females were cohabited nightly with males from the repeat dose component, one male to one female, from the same treatment group, for up to 14 days. Females were evaluated daily for evidence of mating. Once mating was confirmed (GD 0), females were separated from the males for the remainder of gestation, and allowed to deliver and nurse litters until Postnatal Day (PND) 4. Litter size (number of stillborn and live born pups) and pup evaluations (body weight, sexing, and external examination) were recorded at birth and PND 4. Pups were euthanized and externally examined on PND 4 and the carcasses were discarded without further examination. Complete necropsies were performed on all animals; selected organs and tissues were collected, weighed, and preserved. In the developmental component, no effect of treatment was evident for gestation length, litter size, pup body weight, pup sex ratios, pup survival, or pup external examinations to PND 4. The No-Observable-Effect Level (NOEL) for developmental toxicity was 1030 mg/kg/day, the highest dose level evaluated.

#### **4.5 Additional Data**

##### **4.5.1 Metabolism**

Data are available which show that DAC undergoes hydrolysis under biological conditions (Subak and Beauregard, 1981).

##### **4.5.2 Eye and Skin Irritation**

Studies in rabbits have shown that DAC causes skin irritation (of varying degrees of severity) (Ebbens, 1971; Lacroix et al., 1976; Reddington, 1979) and is slightly irritating to eyes (Ebbens, 1971).

##### **4.5.3 Sensitization**

Studies have shown that the skin irritation caused by dermal exposure of rabbits to DAC is not allergic in nature (Humphrey, 1979; Reddington, 1979).

##### **4.5.4 Human Experience**

Studies in humans have shown that DAC causes irritant contact dermatitis (Lacroix et al., 1976; Lovell et al., 1988).

#### **5. Proposed Testing**

There is no proposed testing as valid data are available to satisfy all endpoints.

## 6. Summary

In summary, valid data are present to satisfy all physical/chemistry, ecotoxicity, and environmental endpoints. Additionally, existing studies are sufficient to satisfy the human health endpoints. Data for metabolism, eye and skin irritation, and sensitization are summarized (although not required).

## 7. References

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