Test Plan
for

Propylene Carbonate

CAS Number 108-32-7

USEPA HPV Challenge Program Submission

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Submitted by:

Propylene Carbonate / t-Butyl Alcohol HPV Committee

Members:

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I. Introduction

The Propylene Carbonate / t-Butyl Alcohol HPV Committee and its member companies have committed voluntarily to develop screening level human health effects, environmental fate and effects, and physicochemical test data for propylene carbonate under the Environmental Protection Agency's High Production Volume Challenge Program.

Propylene Carbonate (PC) is produced in a continuous process by the reaction of propylene oxide (PO) with CO_2 and sold as different purity and color grades dependent on the supplier. PC may be used as a solvent for chemical reactions or as a carrier of cosmetically active agents, medicinal agents, biocides, and fungicides. PC may also be used as a reactive intermediate in alkoxylations, transesterifications, polymerizations, reaction with amines, or carboxylic acids. PC is a popular solvent for lithium ion batteries. It is used in the production of electrochromic or "auto-dimming" mirrors for automobiles.

Data Summary

	Data Available	Data Adequate	testing recommended
Melting point	Yes	Yes	No
Boiling point	Yes	Yes	No
Vapor Pressure	Yes	Yes	No
Partition Coefficient	Yes	Yes	No
Water Solubility	Yes	Yes	No
Stability in Water	No	No	Yes
Transport	No	No	Yes
Photodegradation	Yes	Yes	No
Biodegradation	Yes	Yes	No
Acute Toxicity to Fish	Yes	Yes	No
Acute Toxicity to Invert.	Yes	Yes	No
Acute Toxicity to aq.plants	No	No	Yes
Acute Tox – oral	Yes	Yes	No
Acute Tox – dermal	Yes	Yes	No
Gene Tox *in vivo* – MN	Yes	Yes	No
Gene Tox *in vitro* – Ames	Yes	Yes	No
Repeat dose- oral (90 day)	Yes	Yes	No
Repeat dose-inhal (90 day)	Yes	Yes	No
Repeat dose-derm (2 year)	Yes	Yes	No
Reproductive toxicity	Limited	Yes	No
Developmental tox	Yes	Yes	No

II. Test Plan and Rationale

A. Physical Chemical Data

The physical /chemical data for propylene carbonate are found in standard reference works. The underlying data were not found, but additional testing is not justified. Data on the stability of propylene carbonate in water and transport between environmental compartments are not adequate. **Recommended testing:**

1. Stability in Water: OECD Test Guideline 111

   Propylene carbonate may hydrolyze under some conditions; therefore, its stability in water under various pH conditions should be determined.

2. Transport and Distribution between Environmental Compartments: Level 1 EQC Model

   The US EPA has acknowledged that computer modeling techniques are an appropriate method for estimating chemical partitioning among environmental compartments. A widely used fugacity model is the Equilibrium Criterion Model (EQC; Mackay et al., 1996). EPA has indicated that it accepts Level I fugacity data as an estimate of chemical distribution values. In EQC level I, distribution is calculated as percent partitioned to 6 compartments within a unit world. Level I data are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical is likely to partition.

B. ECOTOXICITY

Acute toxicity studies on fish and daphnia on a propylene carbonate analog, butylene carbonate, were conducted according to OECD Guidelines, following GLP guidelines. Butylene carbonate (CAS # 4437-85-8) is considered an acceptable surrogate for propylene carbonate because of similar physical-chemical properties.

In rainbow trout the LC50 for butylene carbonate was 480 mg/l and in Daphnia the EC50 was >1000 mg/l. Based on similarity to butylene carbonate, propylene carbonate is not expected to be significantly more toxic to aquatic organisms. The low toxicity of butylene carbonate provides adequate information to conclude that propylene carbonate is not likely to be more than slightly toxic to aquatic organisms. Additional testing of propylene carbonate is not needed.

A biodegradation study of propylene carbonate was published in German in Git. Fachz. Lab. Based on the English abstract, propylene carbonate is readily biodegradable; more than 80% biodegraded during 10 days. Additional biodegradation data are not needed.

Recommended ecotoxicity testing: Toxicity to Aquatic plants (*e.g.*, Algae): OECD Test Guideline 201

No studies of propylene carbonate toxicity to algae are available; an acute toxicity study in algae is recommended (OECD guideline).

C. MAMMALIAN TOXICITY

Numerous adequate and reliable acute toxicity tests are available on propylene carbonate. Oral and dermal tests meet OECD and EPA test guidelines. Propylene carbonate is practically nontoxic following acute exposures; the oral LD50 is >5000 mg/kg and the dermal LD50 is >3000 mg/kg. No further testing is recommended.

Subchronic studies (13-14 weeks) of propylene carbonate by inhalation (aerosol) and oral (gavage) routes were conducted in rats according to current guidelines. The oral study indicated low systemic toxicity from propylene carbonate (NOAEL = 5000 mg/kg/day). In the inhalation study, no systemic toxicity was seen at concentrations up to 1000 mg/m^3; however, there was periocular irritation and swelling in a few males at 500 and 1000 mg/m^3. A dermal carcinogenicity study in mice did not indicate tumorigenic potential or systemic toxicity from 2 years of exposure to propylene carbonate. No further testing is recommended.

There is a negative Ames *in vitro* mutagenicity assay of propylene carbonate. A single intraperitoneal injection of 1666 mg/kg propylene carbonate did not induce an increase in micronuclei when examined after 30, 48 and 72 hours. The mutagenicity battery is satisfactorily filled; no further mutagenicity testing is recommended.

Gavage administration of propylene carbonate to pregnant rats days 6-15 of gestation resulted in systemic toxicity at doses of 3000 and 5000 mg/kg/day, including mortality (not seen in 13 week study of non-pregnant rats). The NOAEL for maternal toxicity was 1000 mg/kg/day. This indicates that pregnant rats are more susceptible to propylene carbonate than are non-pregnant rats. There were no significant differences in live litter size, average fetal weight, percentage of males, or malformed fetuses. No further developmental toxicity testing is recommended.

No studies of the effect of propylene carbonate on reproduction are available. However, no adverse effects on testis, ovaries, or accessory sex organs were noted in rats following oral or inhalation of propylene carbonate for 13 weeks. Therefore, reproductive effects from propylene carbonate are unlikely and further testing is not recommended.