

## SCREENING-LEVEL HAZARD CHARACTERIZATION 1,3-Dioxolane (CASRN 646-06-0)

The High Production Volume (HPV) Challenge Program<sup>1</sup> 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<sup>1,2</sup>) 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<sup>2,3</sup> 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, EXTTOXNET, 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.

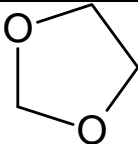
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<sup>1</sup> U.S. EPA. High Production Volume (HPV) Challenge Program; <http://www.epa.gov/chemrtk/index.htm>.

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

<sup>3</sup> 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.

<b>Chemical Abstract Service Registry Number (CASRN)</b>	<b>646-06-0</b>
<b>Chemical Abstract Index Name</b>	<b>1,3-Dioxolane</b>
<b>Structural Formula</b>	
<b>Summary</b>	
<p>This chemical is a liquid with high water solubility and high vapor pressure. It is expected to have high mobility in soil. Volatilization of this chemical from water and moist soils is considered moderate based on its Henry's Law constant. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered moderate. This chemical is expected to have moderate persistence (P2) and low bioaccumulation potential (B1).</p> <p>The acute toxicity of this chemical to rats via oral and inhalation routes is low. This chemical is a skin and eye irritant in rabbits and a skin sensitizer in guinea pigs. Repeated exposures to this chemical via the inhalation route in rats showed changes in organ weights, clinical chemistry and histopathology at 9.12 mg/L/day; the NOAEL for systemic toxicity was 3.03 mg/L/day. Oral one-generation reproductive toxicity studies with rats showed decreased body weights in the adult females and decreased survival of fetuses and pups at 500 mg/kg/day; the NOAEL for reproductive toxicity was 100 mg/kg/day. An oral prenatal developmental toxicity study with rats showed decreased body weight gains in the adult females at 500 mg/kg/day and reduced fetal body weights and skeletal malformations or variations at 1000 mg/kg/day; the NOAEL for maternal and developmental toxicity was 250 mg/kg/day and 500 mg/kg/day, respectively. This chemical did not induce gene mutations or chromosomal aberrations <i>in vitro</i> and did not induce micronuclei <i>in vivo</i>. This chemical did not induce mutations in a dominant lethal assay.</p> <p>The measured 96-hour LC<sub>50</sub> of CASRN 646-06-0 to fish is &gt; 95.4 mg/L, the measured 48-hour EC<sub>50</sub> to aquatic invertebrates is &gt; 772 mg/L, and the measured 96-hour EC<sub>50</sub> to aquatic plants is &gt; 877 mg/L (biomass and growth).</p> <p>There were no data gaps identified under the HPV Challenge Program.</p>	

The sponsor, The Dioxolane Manufacturers Consortium, submitted a Test Plan and Robust Summaries to EPA for 1,3-dioxolane (CASRN 646-06-0; CA Index Name: 1,3-dioxolane) on November 20, 2000. EPA posted the submission on the ChemRTK HPV Challenge Website on December 19, 2000 (<http://www.epa.gov/chemrtk/pubs/summaries/dioxlne/dioxtc.htm>). EPA comments on the original submission were posted on April 18, 2001. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on June 12, 2001, which were posted to the ChemRTK HPV Challenge website on April 3, 2002.

## **1 Chemical Identity**

### **1.1 Identification and Purity**

The following description is taken from the revised Test Plan and Robust Summaries (2001):

CASRN 646-06-0 is a stable reaction product of ethylene glycol and formaldehyde used primarily as a monomer for production of high molecular weight polyacetals. The purity of the test substance ranged from 99.78% to 99.99%.

### **1.2 Physical-Chemical Properties**

The physical-chemical properties of CASRN 646-06-0 and its supporting chemicals are summarized in Table 1. CASRN 646-06-0 is a liquid with high water solubility and high vapor pressure.

<b>Table 1. Physical-Chemical Properties of 1,3-Dioxolane<sup>1</sup></b>	
<b>Property</b>	<b>Value</b>
CASRN	646-06-0
Molecular Weight	74.08
Physical State	Liquid
Melting Point	<b>-95°C (measured)</b>
Boiling Point	<b>78°C (measured)</b>
Vapor Pressure	<b>70 mm Hg at 20°C (measured)</b>
Water Solubility	miscible
Dissociation Constant (pK <sub>a</sub> )	<b>-3.80 (measured)<sup>2</sup></b>
Henry's Law Constant	<b>2.45×10<sup>-5</sup> atm-m<sup>3</sup>/mole (measured)<sup>2</sup></b>
Log K <sub>ow</sub>	<b>-0.37 (measured)</b>

<sup>1</sup>Dioxolane Manufacturer's Consortium. June 12, 2001. Revised Robust Summary and Test Plan for 1,3-Dioxolane. <http://www.epa.gov/hpv/pubs/summaries/dioxlne/dioxtc.htm>.

<sup>2</sup>SRC. The Physical Properties Database (PHYSPROP). Syracuse, NY: Syracuse Research Corporation. Available from <http://www.syrres.com/esc/physprop.htm> as of October 1, 2008.

## **2 General Information on Exposure**

### **2.1 Production Volume and Use Pattern**

This chemical had an aggregated production volume in the United States of 1 million to 10 million pounds during 2005.

Non-confidential information in the Inventory Update Reporting (IUR)<sup>4</sup> indicated that the industrial processing and uses of the chemical include processing as an intermediate in resin and synthetic rubber manufacturing, as well as processing as a solvent in other basic organic chemical manufacturing. Non-confidential information in the IUR indicated that the commercial and consumer products containing the chemical include “other.” The High Production Volume (HPV) submission for this chemical states that it is primarily used as a co-monomer for the manufacture of polyacetals and other polymers, solvent for chemical reactions, stabilizer for halogenated organic solvents, and as a starting material or reagent for organic synthesis.<sup>5</sup> The HSDB states that the major uses of this chemical include a low-boiling solvent and extractant for oils, fats, waxes, dyes and cellulose derivatives.

## 2.2 Environmental Exposure and Fate

Based on use information, there is potential for environmental releases although the quantity and media of releases are unknown. According to the HPV test plan, environmental releases of the chemical could occur from released vapors or from wastewater effluent. The test plan also provided some monitoring data of wastewater and states that all known users of commercial 1,3-dioxolane have an approved wastewater treatment facility on-site.

The environmental fate properties are provided in Table 2. CASRN 646-06-0 is expected to have high mobility in soil. CASRN 646-06-0 was not readily biodegradable using a closed bottle (OECD 301D) test and a 15 day screening level biochemical oxygen demand (BOD) test. The rate of volatilization of CASRN 646-06-0 from water and moist soil is considered moderate based on its Henry’s Law constant. The rate of hydrolysis is considered negligible under environmental conditions. CASRN 646-06-0 is expected to have moderate persistence (P2) and low bioaccumulation potential (B1).

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<sup>4</sup> USEPA, 2006 Inventory Update Reporting Database.

<sup>5</sup> Toxicology and Regulatory Affairs, June 12, 2007. USEPA HPV Challenge Program Submission. Accessed: October 22, 2008. <http://www.epa.gov/chemrtk/pubs/summaries/dioxlne/c12846a.pdf>.

<b>Property</b>	<b>Value</b>
Photodegradation Half-life	11.5 hours (estimated)
Hydrolysis Half-life	<b>&gt;1 year at pH 4, 7, and 9 (measured)</b>
Biodegradation	<b>3.7 % after 35 days (not readily biodegradable); 12% after 15 days (not readily biodegradable)</b>
Bioconcentration	BCF = 3.162 (estimated) <sup>2</sup>
Log K <sub>oc</sub>	0 (estimated) <sup>2</sup>
Fugacity (Level III Model)	Air = 4.11% Water = 54.1% Soil = 41.7% Sediment = 0.0905%
Persistence <sup>3</sup>	P2 (moderate)
Bioaccumulation <sup>3</sup>	B1 (low)

<sup>1</sup>Dioxolane Manufacturer's Consortium. June 12, 2001. Revised Robust Summary and Test Plan for 1,3-Dioxolane. <http://www.epa.gov/hpv/pubs/summaries/dioxlne/dioxtc.htm>.

<sup>2</sup>USEPA. 2008. Estimation Programs Interface Suite™ (version 3.20). United States Environmental Protection Agency, Washington, DC, USA Available online at: <http://www.epa.gov/opptintr/exposure/pubs/episuite.htm>.

<sup>3</sup>Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

### **3 Human Health Hazard**

#### ***Acute Oral Toxicity***

(1) Sprague-Dawley rats (5/sex/dose) were administered single doses of neat CASRN 646-06-0 via gavage at 2500, 3500, 5000, 7100 or 10,000 mg/kg-bw and were observed for 14 days. No mortality was observed at 2500 and 3500 mg/kg-bw. At 5000 mg/kg-bw, one male and two females died. All animals died at the higher doses.

**LD<sub>50</sub> = 5200 mg/kg-bw**

(2) Rats (6, sex and strain not reported) were administered single doses of neat CASRN 646-06-0 via gavage at 1060, 1590, 2390, 3580, 5380 or 8060 mg/kg-bw and were observed for 14 days. Mortality was observed at the highest dose (<http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384>).

**LD<sub>50</sub> > 5380 mg/kg-bw**

#### ***Acute Inhalation Toxicity***

(1) CD® rats (5/sex/concentration) were exposed (whole-body) to CASRN 646-06-0 vapor for 4-hours at nominal concentrations of 0, 37.9, 60.6, 67.9, 88.4 and 201.9 mg/L and were observed for 14 days. All animals at the highest dose died and only one male survived at 88.4 mg/L. At 67.9 mg/L, four males and one female died. At 60.6 mg/L, one female died. No mortality was observed at 37.9 mg/L.

**4-h LC<sub>50</sub> ~ 68.4 mg/L**

(2) Rats (5/concentration/sex not stated) were exposed to CASRN 646-06-0 vapors for 132 minutes at 86,000 ppm (~260 mg/L), 90 minutes at 104,000 ppm (~316 mg/L) and 60 minutes at 82,000 ppm (~248 mg/L); surviving animals observed for 14 days. All animals exposed for 132 minutes died during exposure. One animal exposed for 90 minutes died the first day following exposure and no animals died in the 60 minute exposure group (<http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384>).

**LC<sub>50</sub> ~ 78.6 mg/L**

### ***Repeated-Dose Toxicity***

In a 13-week study, Fischer 344 rats (10/sex/concentration) were exposed (whole body) to CASRN 646-06-0 vapor at 0, 298, 1000 or 3010 ppm (approximately 0.90, 3.03 or 9.12 mg/L/day), 6 hours/day, 5 days/week. There was a reduction in white blood cell counts at all concentrations in male rats which was statistically significant at the medium and high concentrations. In females, there was a decrease in absolute spleen weight at 3010 ppm and relative spleen weights at 1000 and 3010 ppm. In males, relative spleen weights were decreased at 3010 ppm. In females, relative liver weights were increased at 1000 to 3010 ppm and absolute liver weights were increased at 3010 ppm. In males, absolute and relative liver weights were increased at 3010 ppm. Decreased alertness (males and females) and urine specific gravity (males) in animals exposed to the highest concentration of 1,3-dioxolane were also observed. Microscopically, male rats exposed to 3010 ppm 1,3-dioxolane had slightly larger hepatocytes in centrilobular regions and more cytoplasmic eosinophilia were seen than in controls.

**LOAEL ~ 9.12 mg/L** (based on changes in organ weights, clinical chemistry and histopathology)

**NOAEL ~ 3.03 mg/L**

### ***Reproductive Toxicity***

Two of the submitted oral reproductive toxicity studies [(1) and (2)] were conducted at the Industrial Bio-Test Laboratories (IBT), Inc. Based on Section 3.1.8 of the *Manual for Investigation of HPV Chemicals* regarding the acceptance and use of IBT studies ([http://www.oecd.org/document/7/0,2340,en\\_2649\\_34379\\_1947463\\_1\\_1\\_1\\_1,00.html](http://www.oecd.org/document/7/0,2340,en_2649_34379_1947463_1_1_1_1,00.html)), when the study has not been audited by either EPA or FDA, and if the findings of the IBT study were consistent with a study conducted at a later date in another laboratory, then the data may be used but should be considered as weak evidence. In this case, the IBT studies are supported by an independent reference (Sitarek et al., 1992) and data from a dominant lethal assay in rats.

(1) In a one generation reproductive toxicity study, male albino rats (10/dose) were administered CASRN 646-06-0 in drinking water at doses of 0.5 or 1.0% (approximately 500 or 1000 mg/kg-bw/day), 90 days prior to mating with previously untreated females (10/dose) to produce the F1a generation. Controls received water without the test substance. Dosing continued for males and females throughout the mating period and then continued for females throughout gestation, lactation and weaning to produce the F1a generation. These same females were then mated to untreated proven male breeders to produce the F1b generation. Mating with the treated males to produce the F1a litter resulted in treated groups copulating less frequently, fewer pregnant

treated animals delivering litters than controls, a decrease in the number of pups delivered by the high dose group, an increase in the number of stillborn pups in both groups, reduced survival of progeny in the high dose group and a decrease in body weight of dams at the highest dose. Mating with proven breeders to produce the F1b litter showed decreases in the fecundity, parturition and female fertility indices compared to controls.

**LOAEL (reproductive toxicity) ~ 500 mg/kg-bw/day** (based on decreased body weights of dams and decreased survival of fetuses and pups)

**NOAEL (reproductive toxicity) = Not established**

(2) In a one-generation reproductive toxicity study, male albino rats (10/dose) were exposed to CASRN 646-06-0 in drinking water at concentrations of 0.01, 0.03 or 0.1% (approximately 10, 30 and 100 mg/kg-bw/day, respectively) for 90 days prior to mating with previously untreated females. Animals were treated during mating and for females, the treatment continued throughout gestation and lactation. Controls received water without the test substance. No treatment-related effects were seen in this study.

**NOAEL (reproductive toxicity) ~ 100 mg/kg-bw/day**

(3) In the 13-week inhalation study in Fisher 344 rats described previously, evaluations of male organ weights (testes) and histopathology on the epididymides, mammary gland, ovaries, oviducts, prostate, seminal vesicles, testes, uterus and vagina did not show treatment-related effects.

(4) In a dominant lethal assay, male rats were administered CASRN 646-06-0 at 0, 580 or 1160 mg/kg-bw 5 days/week for eight weeks and were mated with virgin females. Pregnant females were euthanized and uterine contents were examined to determine number of implants and live and dead embryos. No evidence of a dominant lethal effect was seen.

### *Developmental Toxicity*

In a prenatal developmental toxicity study, pregnant female rats (25/dose) were dosed at 0, 125, 250, 500 or 1000 mg 1-3-dioxolane/kg-bw/day in corn oil via oral gavage on gestations days 6-15. Maternal toxicity was evident from statistically significant decreased body weight and food consumption at 500 and 1000 mg/kg/day. Developmental toxicity was evident at the highest dose of 1000 mg/kg-bw/day and was characterized by significant increases in litter and fetal incidences of septal defects in the heart and externally evident vertebral malformations associated with tail malformations. One high dose fetus had a cleft palate. Other adverse effects included reduced ossification of centra in the thoracic vertebrae, the lumbar vertebrae, absent sacral and caudal vertebrae and rib-vertebral malformations at this dose level.

**LOAEL (maternal toxicity) = 500 mg/kg-bw/day** (based on decrease in body weight gain)

**NOAEL (maternal toxicity) = 250 mg/kg-bw/day**

**LOAEL (developmental toxicity) = 1000 mg/kg-bw/day** (based on reduced fetal body weights and gross external, soft tissue and skeletal malformations or variations)

**NOAEL (developmental toxicity) = 500 mg/kg-bw/day**

### *Genetic Toxicity – Gene Mutation*

#### *In vitro*

(1) An Ames assay was performed using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, with and without metabolic activation, and CASRN 646-06-0 concentrations of 0.005–50 µL/plate. The test with TA1535 was repeated because of “low solvent counts”. The test material did not induce an increase in mutant frequency in tester strains in the presence or in the absence of metabolic activation. Appropriate positive and negative controls responses were observed in the study.

**CASRN 646-06-0 was not mutagenic in this assay.**

(2) In an Ames assay, *S. typhimurium* TA1535, TA 1537, TA1538 and *Saccharomyces cerevisiae* strain D4 were exposed to CASRN 646-06-0, with and without metabolic activation, at concentrations of 0.75 and 1.50% suspension for *S. typhimurium* and 2.0 and 5.0% suspension for *S. cerevisiae*. The test material did not induce an increase in mutant frequency in tester strains TA 1535, TA1537 or TA1538 or in *S. cerevisiae* in the presence or in the absence of metabolic activation. Appropriate positive and negative control responses were observed in the study.

**CASRN 646-06-0 was not mutagenic in this assay.**

(3) In a forward mutation assay, mouse lymphoma cells (L5 178Y TK+/-) were exposed to CASRN 646-06-0 at 0, 750 to 50,000 nL/mL with and without metabolic activation. Low dose-dependent cytotoxicity was seen. The results indicated no dose-dependent increase in the number of mutants in the presence or absence of metabolic activation. Positive and negative controls responded appropriately.

**CASRN 646-06-0 was not mutagenic in this assay.**

### *Genetic Toxicity – Chromosomal Aberrations*

#### *In vitro*

Duplicate cultures of Chinese hamster ovary cells were exposed, *in vitro*, to CASRN 646-06-0 at 0, 2.0, 3.0, 4.0, and 5 mg/mL with and without metabolic activation. A total of 200 metaphases were scored for aberrations. Cytotoxicity was not observed at any concentration. No increase in the number of aberrations was seen at any concentration of CASRN 646-06-0. The positive and negative controls responded appropriately.

**CASRN 646-06-0 did not induce chromosomal aberrations in this assay.**

#### *In vivo*

(1) In a micronucleus assay, ICR Harlan Sprague-Dawley mice (5/sex/dose) were administered single doses of CASRN 646-06-0 via intraperitoneal injection at 0, 525, 1050 or 2100 mg/kg-bw and were euthanized 72 hours later. Triethylenemelamine (0.25 mg/kg-bw) was used as a positive control. The number of micronuclei/1000 polychromatic erythrocytes was counted for each animal. Mortality was observed at the highest dose. The positive control produced a statistically significant increase in micronuclei, but there was no significant increase in micronuclei for in any of the 1,3-dioxolane treated groups.

**CASRN 646-06-0 did not induce micronuclei in this assay.**

(2) In a dominant lethal assay previously described, male rats were administered CASRN 646-06-0 at 0, 580 or 1160 mg/kg-bw 5 days/week for eight weeks and mated with virgin females. No evidence of a dominant lethal effect was seen.

**CASRN 646-06-0 was not mutagenic in the assay.**

#### ***Additional Information***

##### ***Skin Irritation***

New Zealand White albino rabbits (3/sex) were clipped to expose the back from the shoulders to the lumbar region. The left side was abraded and the right side was left intact. The sites were treated with 0.5 ml CASRN 646-06-0 and covered. The animals were then wrapped in plastic sheeting. The covering was removed following 24 hours of exposure and the test site wiped free of test material. Dermal observations were made 30 minutes later. The animals were evaluated 24 and 72 hours post-exposure. Slight erythema was present on both the intact and abraded skin. (<http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384>)

**CASRN 646-06-0 was slightly irritating to rabbit skin.**

##### ***Eye Irritation***

New Zealand White albino rabbits (3/sex) were treated with 0.1 ml CASRN 646-06-0 in the right eye. The left eye served as the control. The animals were evaluated at 24, 48 and 72 hours post-exposure. All animals exhibited conjunctival redness. Five animals had corneal ulceration and four had corneal opacification and iridial irritation. One animal exhibited a positive score for conjunctival chemosis. All eyes exhibited signs of irritation at study termination.

(<http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384>)

**CASRN 646-06-0 was irritating to rabbit eyes.**

##### ***Skin Sensitization***

In a skin sensitization study with guinea-pigs (no more information provided), CASRN 646-06-0 was a skin sensitizer.

(<http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384>)

**CASRN 646-06-0 was a skin sensitizer in guinea pigs.**

**Conclusion:** The acute toxicity of this chemical to rats via oral and inhalation routes is low. This chemical is a skin and eye irritant in rabbits and a skin sensitizer in guinea pigs. Repeated exposures to this chemical via the inhalation route in rats showed changes in organ weights, clinical chemistry and histopathology at 9.12 mg/L/day; the NOAEL for systemic toxicity was 3.03 mg/L/day. Oral one-generation reproductive toxicity studies with rats showed decreased body weights in the adult females and decreased survival of fetuses and pups at 500 mg/kg-bw/day; the NOAEL for reproductive toxicity was 100 mg/kg-bw/day. An oral prenatal developmental toxicity study with rats showed decreased body weight gains in the adult females at 500 mg/kg-bw/day and reduced fetal body weights and skeletal malformations or variations at 1000 mg/kg-bw/day; the NOAEL for maternal and developmental toxicity was 250 mg/kg-bw/day and 500 mg/kg-bw/day, respectively. This chemical did not induce gene mutations or chromosomal aberrations *in vitro* and did not induce micronuclei *in vivo*. This chemical did not induce mutations in a dominant lethal assay.

## **4 Hazards to the Environment**

### *Acute Toxicity to Fish*

Bluegill sunfish (*Lepomis macrochirus*) were exposed to CASRN 646-06-0 at nominal concentration of 100 mg/L under static conditions for 96 hours with renewal every 24 hours. The mean of the concentration measured at 24, 48, 72 and 96 hours was 95.4 mg/L. No mortality was observed at any concentration.

**96-h LC<sub>50</sub> > 95.4 mg/L**

### *Acute Toxicity to Aquatic Invertebrates*

*Daphnia magna* were exposed to CASRN 646-06-0 at nominal concentrations of 0, 250, 500 and 1000 mg/L under static conditions for 48 hours. Measured concentrations were 213, 411, and 772 mg/L.

**48-h EC<sub>50</sub> > 772 mg/L**

### *Toxicity to Aquatic Plants*

Green algae (*Pseudokirchneriella subcapitata*) were exposed to CASRN 646-06-0 at nominal concentrations of 62.5, 125, 250, 500 and 1000 mg/L for 72 hours. Measured concentrations were 37, 81, 163, 280 and 877 mg/L.

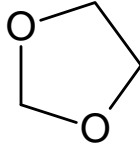
**72-h EC<sub>50</sub> (biomass) > 877 mg/L**

**72-h EC<sub>50</sub> (growth) > 877 mg/L**

**Conclusion:** The measured 96-hour LC<sub>50</sub> of CASRN 646-06-0 to fish is > 95.4 mg/L, the measured 48-hour EC<sub>50</sub> to aquatic invertebrates is > 772 mg/L, and the measured 96-hour EC<sub>50</sub> to aquatic plants is > 877 mg/L (biomass and growth).

## **5 References**

Sitarek K, Baranski B and Berlinska B. The effect of maternal exposure to dioxolane on prenatal and postnatal development in rats. *Pol J Occup Med Environ Health* 5:159-66 (1992).

<b>Table 3. Summary Table of the Screening Information Data Set as submitted under the U.S. HPV Challenge Program</b>	
<b>Endpoints</b>	<b>SPONSORED CHEMICAL 1,3-Dioxolane (CASRN 646-06-0)</b>
<b>Structure</b>	
<b>Summary of Human Health Data</b>	
<b>Acute Oral Toxicity LD<sub>50</sub> (mg/kg-bw)</b>	<b>5200</b>
<b>Acute Inhalation Toxicity LC<sub>50</sub> (mg/L)</b>	<b>68.4</b>
<b>Repeated-Dose Toxicity NOAEL/LOAEL Inhalation (mg/L/day)</b>	<b>(rat) LOAEL ~ 9.12 NOAEL ~ 3.03</b>
<b>Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)</b>	<b>(rat) (1) LOAEL~500 NOAEL = not established</b>
<b>Reproductive</b>	
<b>Reproductive</b>	<b>(2) NOAEL ~ 100</b>
<b>Reproductive Toxicity NOAEL/LOAEL Inhalation (mg/L/day)</b>	No treatment-related effects were seen following evaluation of reproductive organs in the 13-week inhalation repeated-dose study in rats.
<b>Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)</b>	<b>(rat) LOAEL = 500 NOAEL=250 LOAEL = 1000 NOAEL=500</b>
<b>Maternal</b>	
<b>Developmental</b>	
<b>Genetic Toxicity – Gene Mutation <i>In vitro</i></b>	<b>Negative</b>
<b>Genetic Toxicity – Chromosomal Aberrations <i>In vitro</i></b>	<b>Negative</b>
<b>Genetic Toxicity – Chromosomal Aberrations <i>In vivo</i></b>	<b>Negative</b>

<b>Table 3. Summary Table of the Screening Information Data Set as submitted under the U.S. HPV Challenge Program</b>	
<b>Endpoints</b>	<b>SPONSORED CHEMICAL 1,3-Dioxolane (CASRN 646-06-0)</b>
<b>Additional Information</b> Skin Irritation Eye Irritation Skin Sensitization	slightly irritating irritating positive
<b>Summary of Environmental Effects – Aquatic Toxicity Data</b>	
<b>Fish</b> 96-h LC <sub>50</sub> (mg/L)	> 95.4
<b>Aquatic Invertebrates</b> 48-h EC <sub>50</sub> (mg/L)	> 772
<b>Aquatic Plants</b> 72-h EC <sub>50</sub> (mg/L)  (growth) (biomass)	> 877 > 877