

SCREENING-LEVEL HAZARD CHARACTERIZATION
Propanoic acid, 3-(dodecylthio)-, 2,2-bis[[3-(dodecylthio)-1-oxopropoxy]methyl]-1,3-propanediyl ester (CASRN 29598-76-3)

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.

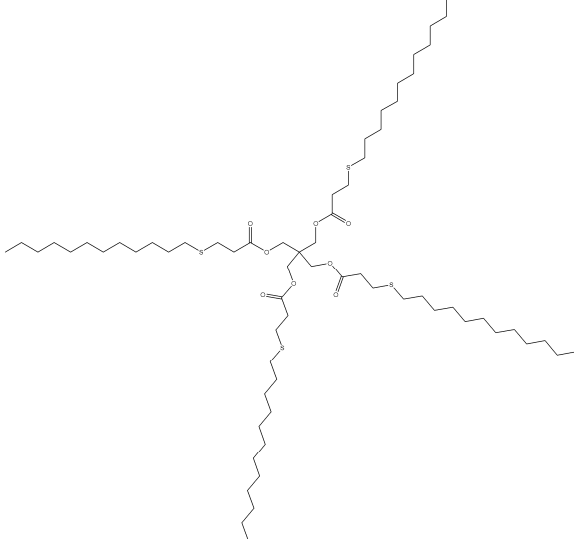
OPPT does not develop HCs for those HPV chemicals which have already been assessed internationally through the HPV program of the Organization for Economic Cooperation and Development (OECD) and for which Screening Initial Data Set (SIDS) Initial Assessment Reports (SIAR) and SIDS Initial Assessment 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>29598-76-3</p>
<p>Chemical Abstract Index Name</p>	<p>Propanoic acid, 3-(dodecylthio)-, 2,2-bis[[3-(dodecylthio)-1-oxopropoxy]methyl]-1,3-propanediyl ester</p>
<p>Structural Formula</p>	
<p style="text-align: center;">Summary</p> <p>The chemical is a solid with negligible water solubility and negligible vapor pressure. It is expected to have low mobility in soil. Volatilization of this chemical is considered low based on its Henry's Law constant. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered rapid; however, it is unlikely that any of this substance will exist in the vapor phase in the ambient atmosphere. The chemical is expected to have high persistence (P3) and low bioaccumulation potential (B1).</p> <p>The acute oral toxicity of the chemical in rats is low. In an oral combined repeated-dose/reproductive/developmental toxicity screening study in rats, the chemical showed effects on the heart in adult animals at 100 mg/kg-bw/day but no effects on reproductive/pre- and postnatal developmental toxicity at the highest dose tested; the NOAEL for systemic toxicity was not established and for reproductive/developmental toxicity was 1000 mg/kg-bw/day. CASRN 29598-76-3 was not mutagenic in bacterial assays and did not induce chromosomal aberrations in mammalian cells <i>in vitro</i>.</p> <p>Based on estimated log K_{ow} (24.8) and water solubility (1.3×10^{-21} mg/L), the acute toxicity of CASRN 29598-76-3 is expected to be "no effects at saturation" for fish, aquatic invertebrates and aquatic plants.</p> <p>There were no data gaps identified under the HPV Challenge Program.</p>	

The sponsor, Chemtura Corporation (formerly Crompton Corporation), submitted a Test Plan and Robust Summaries to EPA for propionic acid, 3-(dodecylthio)-, neopentanetetrayl ester (CASRN 29598-76-3) on August 27, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on October 2, 2003

(<http://www.epa.gov/chemrtk/pubs/summaries/oxopropo/c14713tc.htm>). EPA comments were posted on the original submission on February 4, 2004. Public comments were also received and posted to the website. The sponsor submitted revised documents on March 18, 2004, which were posted to the ChemRTK website on June 30, 2004 and June 15, 2008.

1 Chemical Identity

1.1 Identification and Purity

The following description is taken from the final Test Plan and Robust Summaries (2006):

CASRN 29598-76-3 is an antioxidant for use with polyolefins (particularly polyethylene and polypropylene) and engineering thermoplastics. The purity of the test substance was not stated in the test plan or robust summaries.

1.2 Physical-Chemical Properties

The physical-chemical properties of CASRN 29598-76-3 are summarized in Table 1. CASRN 29598-76-3 is a solid with negligible water solubility and negligible vapor pressure.

Table 1. Physical-Chemical Properties of Propanoic Acid, 3-(Dodecylthio)-, 2,2-Bis[[3-(Dodecylthio)-1-Oxopropoxy]Methyl]-1,3-Propanediyl Ester¹	
Property	Value
CASRN	29598-76-3
Molecular Weight	1161.95
Physical State	Solid
Melting Point	50–51°C
Boiling Point	Decomposes
Vapor Pressure	6.7×10^{-24} mm Hg at 25°C (estimated)
Water Solubility	1.3×10^{-21} mg/L at 25°C (estimated)
Dissociation Constant (pK _a)	Not applicable
Henry's Law Constant	6.3×10^{-17} atm·m ³ /mole (estimated) ²
Log K _{ow}	24.8 (estimated)

¹Crompton Corporation. June 30, 2004. Revised Robust Summary for Propanoic Acid, 3-(Dodecylthio)-, 2,2-Bis[[3-(Dodecylthio)-1-Oxopropoxy]Methyl]-1,3-Propanediyl Ester.

<http://www.epa.gov/oppt/chemrtk/pubs/summaries/oxopropo/c14713tc.htm>.

²US EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v 3.20. United States Environmental Protection Agency, Washington, DC, USA.

<http://www.epa.gov/opptintr/exposure/pubs/episuite.htm>.

2 General Information on Exposure

2.1 Production Volume and Use Pattern

This chemical had an aggregated production and/or imported volume in the United States of less than 500,000 pounds in 2005.

The HPV submission states that the chemical is an antioxidant for use with polyolefins and engineering thermoplastics.⁴

2.2 Environmental Exposure and Fate

No quantitative information is available on releases of this chemical to the environment.

The environmental fate properties are provided in Table 2. This chemical is expected to have low mobility in soil. The rate of biodegradation is considered slow to negligible based on the results of a ready biodegradation test (OECD 301C). The rate of volatilization of this chemical from water and moist soil is considered low based on its estimated Henry's Law constant. The rate of hydrolysis is considered negligible under environmental conditions. It is expected to have high persistence (P3) and low bioaccumulation potential (B1).

Table 2. Environmental Fate Characteristics of Propanoic Acid, 3-(Dodecylthio)-, 2,2-Bis[[3-(Dodecylthio)-1-Oxopropoxy]Methyl]-1,3-Propanediyl Ester¹	
Property	Value
Photodegradation Half-life	0.9 hours (estimated)
Hydrolysis Half-life	>1 year at pH 7 and 25°C (estimated); 59 days at pH 8 and 25°C (estimated)
Biodegradation	4% after 28 days (not readily biodegradable)²
Bioconcentration	BCF = <7 to <84 (measured in carp)²
Log K _{oc}	24.4 (estimated)
Fugacity (Level III Model)	Air = 0.036% Water = 2.38% Soil = 28.9% Sediment = 68.7%
Persistence ³	P3 (high)
Bioaccumulation ³	B1 (low)

¹Crompton Corporation. June 30, 2004. Revised Robust Summary for Propanoic Acid, 3-(Dodecylthio)-, 2,2-Bis[[3-(Dodecylthio)-1-Oxopropoxy]Methyl]-1,3-Propanediyl Ester.

<http://www.epa.gov/oppt/chemrtk/pubs/summaries/oxopropo/c14713tc.htm>.

²National Institute of Technology and Evaluation. 2002. Biodegradation and Bioconcentration of Existing Chemical Substances under the Chemical Substances Control Law.

http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html

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

⁴Crompton Corporation, 2004. HPV Test Plan. Accessed, 10/13/08.

<http://www.epa.gov/chemrtk/pubs/summaries/oxopropo/c14713rt.pdf>.

3 Human Health Hazard

Acute Toxicity

Acute oral toxicity data show that this chemical has low toxicity to rats. Only limited details were provided for this study.

LD₅₀ > 15,000 mg/kg-bw

Repeated-Dose Toxicity

In a combined repeated-dose/reproductive/developmental toxicity screening test, Wistar rats of both sexes (number not stated) were exposed to CASRN 29598-76-3 by oral gavage at 0, 100, 400 or 1000 mg/kg-bw/day. Males were dosed for a minimum of 4 weeks (2 weeks prior to mating, during mating and about 2 weeks following mating). Females were dosed for 2 weeks prior to mating, during mating, gestation and until postnatal day 4. Animals in a recovery group were observed for 14 days after treatment for reversibility, persistence or delayed occurrence of effects. Aspartate aminotransferase (AST) activity was increased in males at all dose groups and in females at 400 and 1000 mg/kg-bw/day. AST activity from the recovery group animals was comparable to the control group at the end of 14 day recovery period. Relative heart weights were increased in males at 400 and 1000 mg/kg-bw/day. Histopathological changes in the heart were observed in both males and females at all doses. Fibrosis in the hearts of the high-dose recovery group animals was observed after cessation of exposure; the severity of the fibrosis was less than that in the treatment groups.

LOAEL = 100 mg/kg-bw/day (based on histopathological changes in the heart in males and females and increased AST levels in males)

NOAEL = Not established

Reproductive Toxicity

In the combined repeated-dose/reproductive/developmental toxicity screening test, described previously, Wistar rats of both sexes (number not stated) were exposed to CASRN 29598-76-3 by oral gavage at 0, 100, 400 or 1000 mg/kg-bw/day. There were no treatment-related effects on gestation and lactation body weights and food consumption, number and weight of pups, survivability of pups or fertility indices.

NOAEL (reproductive toxicity) = 1000 mg/kg-bw/day

Developmental Toxicity

In the combined repeated-dose/reproductive/developmental toxicity screening test, described previously, female Wistar rats were exposed to CASRN 29598-76-3 by oral gavage at 0, 100, 400 or 1000 mg/kg-bw/day until postnatal day 4. There were no treatment-related effects on pup mortality or observations of external abnormalities of live and dead pups at any of the treated doses.

LOAEL (maternal toxicity) = 100 mg/kg-bw/day (based on histopathological changes in the heart)

NOAEL (maternal toxicity) = Not established

NOAEL (developmental toxicity) = 1000 mg/kg-bw/day

Genetic Toxicity – Gene Mutation

In vitro

A bacterial reverse mutation assay was conducted using *Salmonella typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537 and *Escherichia coli* WP2 uvrA with and without metabolic activation and test substance concentrations from 50 to 5000 µg/plate. The positive controls were included in the assay and gave an appropriate response. CASRN 29598-76-3 did not induce mutagenic activity in the presence or absence of metabolic activation.

CASRN 29598-76-3 was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberration

In vitro

Cultured Chinese hamster ovary (CHO) cells were treated with CASRN 29598-76-3 up to 5000 µg/mL in the presence and absence of metabolic activation. The positive controls were included in the test and gave an appropriate response. The test substance did not induce chromosomal aberrations.

CASRN 29598-76-3 was not mutagenic in this assay.

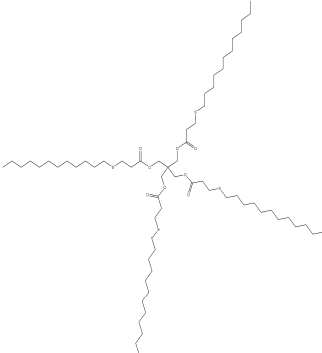
Conclusion: The acute oral toxicity of the chemical in rats is low. In an oral combined repeated-dose/reproductive/developmental toxicity screening study in rats, the chemical showed effects on the heart in adult animals at 100 mg/kg-bw/day but no effects on reproductive/pre- and postnatal developmental toxicity at the highest dose tested; the NOAEL for systemic toxicity was not established and for reproductive/developmental toxicity was 1000 mg/kg-bw/day. CASRN 29598-76-3 was not mutagenic in bacterial assays and did not induce chromosomal aberrations in mammalian cells *in vitro*.

4 Hazards to the Environment

No measured data were submitted for aquatic toxicity. EPA did not recommend testing in its test plan comments because no aquatic toxicity is expected for this chemical at or below water saturation because of the very low estimated water solubility of the chemical (1.3×10^{-21} mg/L at 25°C; estimated by EPIWIN).

Conclusion: Based on estimated log K_{ow} (24.8) and water solubility (1.3×10^{-21} mg/L), the acute toxicity of CASRN 29598-76-3 is expected to be “no effects at saturation” for fish, aquatic invertebrates and aquatic plants.

**Table 3. Summary Table of the Screening Information Data Set
as submitted under the U.S. HPV Challenge Program**

Endpoints	SPONSORED CHEMICAL Propanoic acid, 3-(dodecylthio)-, 2,2-bis[[3-(dodecylthio)-1-oxopropoxy]methyl]-1,3-propanediyl ester (CASRN 29598-76-3)
Structure	
Summary of Human Health Data	
Acute Oral Toxicity LD₅₀ (mg/kg-bw)	> 15,000
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	NOAEL = Not established LOAEL = 100
Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	NOAEL = 1000 (hdt)
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	NOAEL = 1000 (hdt)
Genetic Toxicity - Gene Mutation <i>In vitro</i>	Negative
Genetic Toxicity - Chromosomal aberrations <i>In vitro</i>	Negative
Summary of Environmental Effects – Aquatic Toxicity Data	
<p>No measured data are available for aquatic toxicity and EPA did not recommend any testing in its test plan comments because no aquatic toxicity is expected for this chemical at or below its water solubility limit based on the submitted EPIWIN estimate (1.3×10^{-21} mg/L at 25°C).</p>	

hdt = highest dose tested