

SCREENING-LEVEL HAZARD CHARACTERIZATION

Polybutylene Succinic Anhydride Category

Polyisobutylene succinic anhydride

CASRN 67762-77-0

Polybutenyl succinic anhydride

CASRN 67762-79-2

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, 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

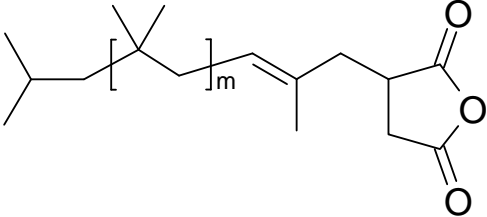
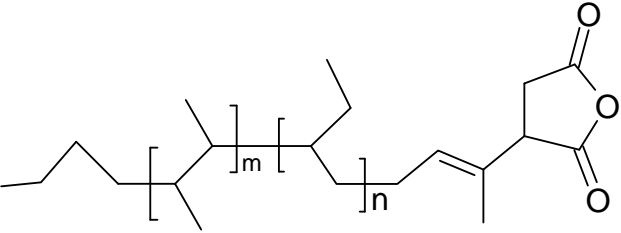
¹ U.S. EPA. High Production Volume (HPV) Challenge Program; <http://www.epa.gov/chemrtk/index.htm>.

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>.

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.

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</p>	<p>67762-77-0 67762-79-2</p>
<p>Chemical Abstract Index Name</p>	<p>Polyisobutylene succinic anhydride Polybutenyl succinic anhydride</p>
<p>Structural Formula</p>	<div style="text-align: center;">  <p>(mw = 519-2483)</p>  <p>(mw = 500-2500)</p> </div>
<p style="text-align: center;">Summary</p> <p>Polybutylene succinic anhydrides are liquids that are expected to have low water solubility and negligible vapor pressure for the lowest MW fraction (500 Dalton) while the highest MW fraction would have negligible water solubility and vapor pressure. Polybutylene succinic anhydrides are expected to have low mobility in soil. The rate of volatilization is expected to be low based on the low Henry's Law constants and strong adsorption to soils, suspended solids, and sediments in water. These compounds contain the anhydride functional group, indicating that the rate of hydrolysis is rapid; however, this rate may be attenuated by the low water solubility of these compounds. The rate of photooxidation is considered rapid; however, polybutylene succinic anhydrides are not expected to exist in the vapor phase in the atmosphere. Polybutylene succinic anhydrides are expected to have moderate persistence (P2) and low bioaccumulation potential (B1).</p> <p>The acute oral and dermal toxicity of CASRNs 67762-77-0 and 67762-79-2 to rats and rabbits, respectively, is low. No data were provided to assess the repeated-dose, reproductive and developmental toxicity of the category members. CASRNs 67762-77-0 and 67762-79-2 did not induce gene mutations in bacteria <i>in vitro</i>. No data were provided for the chromosomal aberration endpoint.</p>	

The acute toxicity to fish, aquatic invertebrates, and toxicity to aquatic plants for CASRNs 67762-77-0 and 67762-79-2 cannot be evaluated because no adequate data were available on the aquatic toxicity of these chemicals.

The repeated-dose/reproductive/developmental toxicity, genetic toxicity (chromosomal aberrations) and chronic toxicity to aquatic invertebrates endpoints are identified as data gaps under the HPV Challenge Program.

The sponsor, the American Chemistry Council, Petroleum Additives Panel, Health, Environmental and Regulatory Task Group (HERTG), submitted a Test Plan and Robust Summaries to EPA for the polybutylene succinic anhydride category on November 27, 2002. EPA posted the submission on the ChemRTK HPV Challenge website on December 20, 2002 (<http://www.epa.gov/chemrtk/pubs/summaries/polybuty/c14084tc.htm>). EPA comments on the original submission were posted to the website on April 23, 2003. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on May 23, 2003 and January 6, 2006 which were posted to the ChemRTK website on June 24, 2003 and March 15, 2006, respectively.

Category Justification

The category covers two substances, each containing mixed monoalkyl succinic anhydrides. The alkyl portion of these anhydrides is either a polyisobutylene (CASRN 67762-77-0) or a polybutenyl (CASRN 67762-79-2) group of varying lengths yielding molecular weight ranges of 500 – 2500. These substances contain the monoalkyl succinic anhydrides as the major constituent, with a residual amount of polybutenes present (content undefined).

The category was primarily based on the structural similarity of the monoalkyl succinic anhydrides and the expectation of similar physical-chemical, environmental fate and toxicological properties. Based on a review of existing information for the anhydrides, the sponsor suggested that monoalkyl succinic anhydrides will undergo hydrolysis and the hydrolyzed products (butanedioic acid, polybutenyl derivatives) will be the forms that should be considered when evaluating environmental fate. In addition to the functional similarity between the anhydrides, the sponsor proposed that the physical-chemical, environmental fate and toxicological properties of the proposed category members are similar. Therefore, the sponsor proposed to use tetrapropenyl butane dioic acid (CASRN 27859-58-1) as a supporting chemical. With a lack of data on the rate of hydrolysis and a significant difference in the molecular sizes between the proposed supporting chemical and the sponsored chemicals, tetrapropenyl butane dioic acid was deemed to be an inadequate supporting chemical.

In the revised submission, the sponsor dropped the supporting chemical and instead proposed that repeated-dose, reproductive and developmental toxicity testing were not needed, given the physical and chemical properties of the chemicals in the category. The sponsor provided the following three supporting arguments:

First, the Polyisobutylene Succinic Anhydride category members will undergo hydrolysis to succinic acid derivatives of low toxicological concern. However, no supporting data were provided. While the original test plan proposed a hydrolysis study on the sponsored substance or a robust summary based on literature data, the revised version did not mention this and provided no data or robust summary on the hydrolysis products, succinic acid.

Second, the test plan argues that data for succinic acid support a low toxicity characterization of the sponsored substances. Use of repeated-dose, reproductive and developmental toxicity data for succinic acid to characterize polybutylene succinic anhydrides is not appropriate because of the very large differences in molecular weight of the dioic acid compared to the category

members. Because the sponsor has not provided adequate justification for using succinic acid data, this hazard characterization considers only the data for the sponsored chemicals for satisfaction of human health and aquatic toxicity endpoints.

Third, the sponsor suggested that there was significant evidence in the literature indicating that members of the polybutylene succinic anhydride category have molecular weights > 1000 (revised upward from 500-2500 in the original submission) with < 25% of the material present below 1000 and thus they are too large and hydrophobic to be absorbed in the intestinal lumen and concluded that testing is not necessary since polybutylene succinic anhydrides would likely show minimal toxicity in repeated-dose and reproductive/developmental toxicity studies.

While the revised test plan referenced EPA's Polymer Exemption Guidance Manual (1997), there was no systematic use of all the relevant exemption criteria to support its position. Although the polymer exemption criteria could provide useful guidance, the test plan did not address such factors as how molecular weights (MWs) were expressed (number average vs. weight average), per cent content below 500 daltons, and the effect of the anhydride function. The sponsors who truly have products that meet the polymer exemption criteria (number average MW > 1000 Da and oligomeric content with 25% below 1000 Da and 10% < 500 Da) could reasonably be exempted from the HPV Challenge testing requirements for health effects. However, any product with lower number average MW (< 1000 Da) or higher oligomeric content would still be considered subject to the requirements of the HPV Challenge program.

Lacking adequate discussion of the points noted above, the sponsor's arguments are insufficient to satisfy the data gaps.

1. Chemical Identity

1.1 Identification and Purity

The polybutylene succinic anhydride category is comprised of two polymeric compounds, 2,5-furandione, dihydro-, monopolyisobutylene derivs. (CASRN 67762-77-0) and 2,5-furandione, dihydro-, monopolybutenyl derivs. (CASRN 67762-79-2).

1.2 Physical-Chemical Properties

The physical-chemical properties of the polybutylene succinic anhydride category members are summarized in Table 1.

Polybutylene succinic anhydrides are relatively low molecular weight (500 – 2500 Dalton) liquids that are expected to have low water solubility and negligible vapor pressure for the lowest MW fraction (500 Dalton) while the highest MW fraction would have negligible water solubility and vapor pressure. In association with water the chemicals will quickly react to form the succinic diacid.

Property	SPONSORED CHEMICAL 2,5-Furandione, dihydro-, monopolyisobutylene derivs.	SPONSORED CHEMICAL 2,5-Furandione, dihydro-, monopolybutenyl derivs.
	Value	Value
CASRN	67762-77-0	67762-79-2
Molecular Weight	519-2483 ²	500-2500 ²
Physical State	Dark colored viscous liquid	Dark colored viscous liquid
Melting Point	<25°C (based on physical state)	<25°C (based on physical state)
Boiling Point	Decomposes	Decomposes
Vapor Pressure	<1×10 ⁻¹⁰ mm Hg at 25°C (estimated) ^{4,5}	<1×10 ⁻¹⁰ mm Hg at 25°C (estimated) ^{4,5}
Water Solubility	< 10 mg/L ³ <1×10 ⁻⁶ mg/L (estimated) ^{4,5}	< 10 mg/L ³ <1×10 ⁻⁶ mg/L (estimated) ^{4,5}
Dissociation Constant (pK _a)	Not applicable	Not applicable
Henry's Law Constant	<1×10 ⁻¹⁰ atm-m ³ /mole (estimated) ^{4,5}	<1×10 ⁻¹⁰ atm-m ³ /mole (estimated) ^{4,5}
Log K _{ow}	>7 (estimated) ^{4,5}	>7 (estimated) ^{4,5}

¹ American Chemistry Council. 2005. Revised Test Plan and Robust Summary for Polybutylene succinic anhydride category. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/polybuty/c14084tc.htm> as of July 2, 2010.

² According to the sponsor, the molecular weights of these substances are >1,000 g/mol in applications used by the consortium member companies.

³ Furia, T.E., Ed. 1972. CRC Handbook of Food Additives. 2nd Edition. Cleveland: The Chemical Rubber Co., p. 232. as reported in Robust Summaries

⁴ U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online at <http://www.epa.gov/opptintr/exposure/pubs/episuitedi.htm> as of July, 2010.

⁵ Values are based on estimations performed for representative structures with six repeating units (mw = 546.91 g/mol) and 18 repeating units (mw = 1220.18 g/mol) (see appendix). Larger molecular weight structures are expected to give similar results.

2. General Information on Exposure

2.1 Production Volume and Use Pattern

The polybutylene succinic anhydride category chemicals had an aggregated production and/or import volume in the United States between 150 million pounds and 600 million pounds in calendar year 2005.

- CASRN 67762-77-0: 100 to <500 million pounds;
- CASRN 67762-79-2: 50 to <100 million pounds;

CASRN 67762-77-0:

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include other basic organic chemical manufacturing as intermediates; all other

chemical product preparation manufacturing as lubricants. Non-confidential commercial and consumer uses of this chemical include lubricants, greases and fuel additives.

CASRN 67762-79-2:

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include all other chemical product preparation manufacturing as lubricants. Non-confidential commercial and consumer uses of this chemical include lubricants, greases and fuel additives.

2.2 Environmental Exposure and Fate

The environmental fate properties of polybutylene succinic anhydrides category members are provided in Table 2.

Polybutylene succinic anhydrides are expected to have low mobility in soil. The category member 2,5-furandione, dihydro-, monopolyisobutylene derivs. (CASRN 67762-77-0) was found to be not readily biodegradable (2.3–5.0% degradation in 4 weeks) using a modified Sturm test (OECD 301B). Based on this test result, the category member 2,5-furandione, dihydro-, monopolybutenyl derivs. (CASRN 67762-79-2) is also expected to be not readily biodegradable based on its similar chemical structure. Volatilization of polybutylene succinic anhydrides is expected to be low given their estimated Henry's Law constants. The sponsor indicates that the polybutylene succinic anhydrides will undergo rapid hydrolysis in the environment to form the corresponding dicarboxylic acids; however, measured rate data are not provided. These structures do contain the anhydride functional group which is susceptible to rapid hydrolysis; however, the polymers in this category are considered to be insoluble in water due to their long hydrophobic tails and, therefore, the rate of hydrolysis may be attenuated. In the absence of measured data, the rate of hydrolysis of polybutylene succinic anhydrides in the environment cannot be predicted with certainty. Polybutylene succinic anhydrides are expected to have moderate persistence (P2) and low bioaccumulation potential (B1).

Property	SPONSORED CHEMICAL 2,5-Furandione, dihydro-, monopolyisobutylene derivs.	SPONSORED CHEMICAL 2,5-Furandione, dihydro-, monopolybutenyl derivs.
	Value	Value
CASRN	67762-77-0	67762-79-2
Photodegradation Half-life	0.8–1.3 hours (estimated) ²	0.9–1.1 hours (estimated) ²
Hydrolysis Half-life	Hydrolyzes to form the dicarboxylic acid ³	Hydrolyzes to form the dicarboxylic acid ³
Biodegradation	2.3–5.0% after 4 weeks (not readily biodegradable)	No data
Bioaccumulation Factor	BAF = 0.89–2.2 (estimated) ^{2,4}	BAF = 0.89–2.1 (estimated) ^{2,4}
Log K _{oc}	>6 (estimated) ^{2,4}	>6 (estimated) ^{2,4}
Fugacity (Level III Model) ^{2,4}		
Air (%)	<1	<1
Water (%)	7–63	7–63
Soil (%)	37–93	37–93
Sediment (%)	<1	<1
Persistence ⁵	P2 (moderate)	P2 (moderate)
Bioaccumulation ⁵	B1 (low)	B1 (low)

¹ American Chemistry Council. 2005. Revised Test Plan and Robust Summary for Polybutylene succinic anhydride category. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/polybuty/c14084tc.htm> as of July 2, 2010.

² U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: <http://www.epa.gov/opptintr/exposure/pubs/episuitedi.htm> as of July, 2010.

³ Structures contain the anhydride functional group which is susceptible to hydrolysis; however, measured rate data are not available. The rate of hydrolysis may be attenuated by the low water solubility of these compounds.

⁴ Values are based on estimations performed for representative structures with 6 repeating units (mw = 546.91 g/mol) and 18 repeating units (mw = 1220.18 g/mol) (see appendix). Larger molecular weight structures are expected to give similar results.

⁵ Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

Conclusion: Polybutylene succinic anhydrides are low molecular weight liquid polymers that are expected to have low water solubility and negligible vapor pressure for the lowest MW fraction (500 Dalton) while the highest MW fraction would have negligible water solubility and vapor pressure. Polybutylene succinic anhydrides are expected to have low mobility in soil. The rate of volatilization is expected to be low based on the low Henry's Law constants and strong adsorption to soils, suspended solids, and sediments in water. These compounds contain the anhydride functional group, indicating that the rate of hydrolysis is rapid; however, this rate may be attenuated by the low water solubility of these compounds. The rate of photooxidation is considered rapid; however, polybutylene succinic anhydrides are not expected to exist in the vapor phase in the atmosphere. Polybutylene succinic anhydrides are expected to have moderate persistence (P2) and low bioaccumulation potential (B1).

3. Human Health Hazard

A summary of health effects data submitted for SIDS endpoints is provided in Table 3.

Polyisobutylene succinic anhydride (CASRN 67762-77-0)

Sprague-Dawley rats (5/sex/dose) were administered polyisobutylene succinic anhydride via gavage at 5000 mg/kg and observed for 14 days following dosing. No mortality was observed during the study.

LD₅₀ > 5000 mg/kg

Polybutenyl succinic anhydride (CASRN 67762-79-2)

Male Wistar rats (10/dose) were administered polybutenyl succinic anhydride via gavage at 500, 7120, 10,140 or 14,430 mg/kg and observed for 14 days following dosing. There was no mortality observed at any dose level.

LD₅₀ > 14,900 mg/kg

Acute Dermal Toxicity

Polyisobutylene succinic anhydride (CASRN 67762-77-0)

CrI:CD®(SD)BR rats (5/sex/dose) were administered polyisobutylene succinic anhydride via the dermal route at 2000 mg/kg (0.014 g/cm²) under semi-occluded conditions for 24 hours and observed for 14 days following dosing. No mortality was observed.

LD₅₀ > 2000 mg/kg

Polybutenyl succinic anhydride (CASRN 67762-79-2)

Male New Zealand White rabbits (4/dose) were administered polybutenyl succinic anhydride via the dermal route at 20,000 mg/kg-bw under abraded (two of four rabbits) and semi-occluded (four of four rabbits) conditions for 24 hours and observed for 14 days following dosing. No mortality was observed.

LD₅₀ > 20,000 mg/kg

Repeated-Dose/Reproductive/Developmental Toxicity

No data were submitted for these endpoints.

Genetic Toxicity – Gene Mutation

In vitro

Polyisobutylene succinic anhydride (CASRN 67762-77-0)

(1) *Salmonella typhimurium* strains TA98 and TA100 and *Escherichia coli* strains WP2uvrA were exposed to polyisobutylene succinic anhydride concentrations of 100, 250, 500, 1000, 5000 and 10,000 µg/plate in Pluronic F127 (25% w/w in ethanol) in the presence and absence of metabolic activation. No evidence of mutagenic activity was reported. Positive and vehicle controls were tested concurrently and responded appropriately. No cytotoxicity was observed up to 10,000 µg/plate with or without activation. Test material precipitate was observed at concentrations of > 250 µg/plate.

CASRN 67762-77-0 was not mutagenic in this assay.

Polybutenyl succinic anhydride (CASRN 67762-79-2)

Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to polybutenyl succinic anhydride concentrations of 100, 250, 500, 1000, 5000 and 10,000 µL/plate in ethanol, in the presence and absence of metabolic activation. No evidence of mutagenic activity was reported. Negative, vehicle and positive controls were tested concurrently and responded appropriately. No cytotoxicity was observed.

CASRN 67762-79-2 was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

No data were submitted for this endpoint.

Conclusion: The acute oral toxicity of the category members, CASRNs 67762-77-0 and 67762-79-2, to rats is low and acute dermal toxicity to rabbits is low. No data were provided to assess the repeated-dose, reproductive and developmental toxicity of the category members. CASRNs 67762-77-0 and 67762-79-2 did not induce gene mutations in bacteria. No data were provided for the chromosomal aberration endpoint.

Table 3. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data		
Endpoints	SPONSORED CHEMICAL Polyisobutylene succinic anhydride (67762-77-0)	SPONSORED CHEMICAL Polybutenyl succinic anhydride (67762-79-2)
Acute Oral Toxicity LD₅₀ (mg/kg)	> 5000	> 14,900
Acute Dermal Toxicity LD₅₀ (mg/kg)	> 2000	> 20,000
Repeated-Dose Toxicity NOAEL/LOAEL (mg/kg-bw/day)	No Data	No Data
Reproductive/Developmental Toxicity NOAEL/LOAEL (mg/kg-bw/day)	No Data	No Data
Genetic Toxicity – Gene Mutation <i>In vitro</i>	Negative	Negative

Measured data in bold text

4. Hazard to the Environment

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 4.

Acute Toxicity to Fish

No adequate data were submitted for this endpoint.

Acute Toxicity to Aquatic Invertebrates

No adequate data were submitted for this endpoint.

Toxicity to Aquatic Plants

No adequate data were submitted for this endpoint.

Conclusion: The acute toxicity to fish, aquatic invertebrates, and toxicity to aquatic plants for CASRNs 67762-77-0 and 67762-79-2 cannot be evaluated because no adequate data were available on the aquatic toxicity of these chemicals.

Table 4. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program –Aquatic Toxicity Data		
Endpoints	SPONSORED CHEMICAL Polyisobutylene succinic anhydride (67762-77-0)	SPONSORED CHEMICAL Polybutenyl succinic anhydride (67762-79-2)
Fish 96-h LC₅₀ (mg/L)	No Data	No Data
Aquatic Invertebrates 48-h EC₅₀ (mg/L)	No Data	No Data
Aquatic Plants 72-h EC₅₀ (mg/L)	No Data	No Data
Chronic Toxicity to Invertebrates 21-day EC₅₀ (mg/L)	No Data	No Data