

SCREENING-LEVEL HAZARD CHARACTERIZATION

Alkyl Diphenyl Oxide Disulfonates (ADPODS) Category

SPONSORED CHEMICALS

C10 Linear ADPODS, Sodium Salt	CASRN 36445-71-3
C16 Linear ADPODS, Sodium Salt	CASRN 65143-89-7
C10 Linear ADPODS, Acid	CASRN 70191-75-2
C12 Branched ADPODS, Acid	CASRN 119345-03-8
C12 Branched ADPODS, Sodium Salt	CASRN 119345-04-9
C6 Linear ADPODS, Sodium salt	CASRN 147732-60-3
C12 Linear ADPODS, Sodium Salt	CASRN 149119-20-0

SUPPORTING CHEMICAL

C9 and C10 (Benax 3B1)	No CASRN
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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

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>.

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.

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 style="text-align: center;"><u>Sponsored Chemicals</u></p> <p style="text-align: center;">36445-71-3 65143-89-7 70191-75-2 119345-03-8 119345-04-9 147732-60-3 149119-20-0</p> <p style="text-align: center;"><u>Supporting Chemicals</u></p> <p style="text-align: center;">No CASRN</p>
<p>Chemical Abstract Index Name</p>	<p style="text-align: center;"><u>Sponsored Chemicals</u></p> <p>Benzenesulfonic acid, decyl(sulfophenoxy)-, sodium salt (1:2] Benzenesulfonic acid, hexadecyl(sulfophenoxy)-, sodium salt (1:2] Benzenesulfonic acid, decyl(sulfophenoxy)-] Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated] Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated, sodium salts] Benzene, 1,1'-oxybis-, sec-hexyl derivs., sulfonated, sodium salts] Benzene, 1,1'-oxybis-, sec-dodecyl derivs., sulfonated, sodium salts]</p> <p style="text-align: center;"><u>Supporting Chemical</u></p> <p style="text-align: center;">C9 and C10 (Benax 3B1)</p>
<p>Structural Formula</p>	<p style="text-align: center;">See Section 1</p>
<p style="text-align: center;">Summary</p> <p>The alkyl diphenyl oxide disulfonates (ADPODS) are solid substances with negligible vapor pressure that tend to be dispersible in water. The ADPODS are expected to have low mobility in soil. Volatilization of the ADPODS category members is not expected to be an important environmental fate process since many of the compounds are sodium salts and acid forms that will exist as anions under environmental conditions. The rate of hydrolysis is negligible for all category members. The rate of atmospheric photooxidation is moderate; however, these</p>	

compounds are not expected to exist in the vapor phase. The members of the ADPODS category are expected to have moderate persistence (P2) and low bioaccumulation potential (B1) with the exception of benzenesulfonic acid, hexadecyl(sulfophenoxy)-, sodium salt (1:2), which may possess high bioaccumulation potential (B3).

Human Health Hazard

The acute oral toxicity is low and the acute dermal toxicity is moderate in rats for all category members. In an oral repeated-dose toxicity study with CASRN 147732-60-3, inflammation of the glandular gastric mucosa was observed at 250 mg/kg/day; the NOAEL for systemic toxicity was 50 mg/kg/day. In a 92-day dietary repeated-dose toxicity study, the supporting chemical, C9 and C10 (Benax 3B1), showed increased serum glutamate pyruvate transaminase and organ weights, a decrease in body weights and reversible histological changes at 1000 mg/kg/day; the NOAEL for systemic toxicity was 500 mg/kg/day. In a 95-day dietary repeated-dose toxicity study in dogs, CASRN 36445-71-3 showed growth depression and increased portal cellularity in the liver of males at 279 mg/kg/day. Female dogs had slight cloudy swelling of the hepatic cells at 325 mg/kg/day. The NOAEL for systemic toxicity in dogs was 163 mg/kg/day (male) and 177 mg/kg/day (female). A 90-day dietary repeated-dose toxicity study in rats with CASRN 119345-04-9, showed central lobular necrosis of parenchymal cells and fatty degeneration in males at 500 mg/kg/day. At the same dose, females showed growth retardation with a statistically significant increase in average liver and kidney weights; the NOAEL for systemic toxicity was 150 mg/kg/day. In a 95-day repeated-dose toxicity study with CASRN 119345-04-9 in dogs, a decrease in body weight gain and clinical chemistry changes were seen at 350 mg/kg/day; the NOAEL for systemic toxicity was 131 mg/kg/day. In a two-year continuous feeding study with CASRN 119345-04-9 in dogs, a decrease in growth and body weight gain were observed at 319 mg/kg/day; the NOAEL for systemic toxicity was 128 mg/kg/day. A 90-day oral repeated-dose toxicity study in rats with CASRN 65143-89-7 showed a significant increase in kidney weights in females at 200 mg/kg/day and above; and in the males at 200 mg/kg/day; the NOAEL for systemic toxicity was 100 mg/kg/day. A combined repeated-dose/reproductive/developmental toxicity study in rats with CASRN 65143-89-7 showed mortality in male rats at 25 mg/kg/day and in females at 75 mg/kg/day. No treatment-related effects were observed on reproductive or developmental endpoints. The NOAEL for systemic toxicity was 25 mg/kg/day and the NOAEL for reproductive/developmental toxicity was 250 mg/kg/day (highest dose tested). A 90-day continuous feeding study with CASRN 65143-89-7 in dogs showed no treatment related effects; the NOAEL for systemic toxicity was 200 mg/kg/day (highest dose tested). In a combined reproductive/developmental toxicity screening test with CASRN 65143-89-7 in rats, no effects on reproductive or developmental parameters were observed; the NOAEL for reproductive/developmental toxicity was 91.75 mg/kg/day (highest dose tested). In a combined oral reproductive/developmental toxicity screening test with CASRN 147732-60-3 in rats, mortality was observed at 1000 mg/kg/day in both sexes; the NOAEL for systemic toxicity was 200 mg/kg/day. There were no treatment related effects on reproductive performance; the NOAEL for reproductive toxicity was 1000 mg/kg/day (highest dose tested). However, pup weights were significantly reduced at 1000 mg/kg/day; the NOAEL for developmental toxicity was 200 mg/kg/day. CASRN 147732-60-3 did not induce genetic mutations in bacteria *in vitro*. CASRN 147732-60-3 induced chromosomal aberrations in human lymphocytes but not in rat lymphocytes *in vitro*. CASRN 65143-89-7 did not induce genetic mutations in bacteria, human lymphocytes, rat lymphocytes or Chinese Hamster Ovary cells *in vitro*. CASRNs 147732-60-3,

149119-20-0 and 119345-03-8 are irritating to the rabbit skin and eye. CASRN 36445-71-3 is irritating to the rabbit eye. CASRN 147732-60-3 is not a skin sensitizer in guinea pigs. CASRN 65143-89-7 is a skin and eye irritant in rabbits and not a skin sensitizer in guinea pigs. CASRN 119345-04-9 is irritating to the rabbit eye. CASRN 119345-04-9 did not show increased incidence of tumors in rats.

No data gaps were identified under the HPV Challenge Program.

Hazard to the Environment

The fish 96-h LC₅₀ for CASRN 36445-71-3 is 1.83 mg/L. The fish 96-h LC₅₀ for CASRN 149119-20-0 is 0.47 mg/L. The aquatic invertebrate 48-h EC₅₀ for CASRN 149119-20-0 is 2.3 mg/L. The 48-h aquatic invertebrate EC₅₀ value for CASRN 65143-89-7 is 6.95 mg/L. The toxicity to aquatic plants 72-h E_bC₅₀ for CASRN 65143-89-7 is 42 mg/L. The 32-d MATC chronic toxicity range for fish for CASRN 119345-03-8 is 0.0125-0.0181 mg/L.

No data gaps were identified under the HPV Challenge Program.

The sponsor, the Dow Chemical Company, submitted a Test Plan and Robust Summaries to EPA for the alkyl diphenyl oxide disulfonates (ADPODS) category on December 20, 2002. EPA posted the submission on the ChemRTK HPV Challenge website on January 22, 2003 (<http://www.epa.gov/chemrtk/pubs/summaries/adpods/c14165tc.htm>). EPA comments on the original submission were posted to the website on June 5, 2003. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on August 26, 2003 and November 15, 2006, which were posted to the ChemRTK website on October 29, 2003 and December 22, 2006, respectively.

Category Justification

The sponsor proposed a category of seven substances containing predominantly monoalkylated derivatives of diphenyl oxide disulfonates. The inclusion of CASRN 28519-02-0 in this category is unclear. However, it is identified by the Sponsor as CASRN 119345-04-9, which is assessed as a category member in this hazard characterization. Each phenyl group of the diphenyl oxide contains a linear or branched alkyl group with carbon numbers of C10 or C12. The alkyl groups are linear aliphatic hydrocarbons, which are bonded to the phenyl groups through the second carbon in the aliphatic hydrocarbon chain. These substances also contain the following minor components: dialkylated derivatives of diphenyl oxide disulfonate and mono- and dialkylated derivatives of diphenyl oxide monosulfonates. The sponsor justifies the category based upon structural similarity of the compounds and similar physiochemical, environmental fate, ecological and toxicological properties. The category members have similar chemical precursors and degradation products. EPA agrees that the category is supported.

Supporting Chemical Justification

Data for Benax 3B1 were used to support repeated-dose toxicity endpoints for CASRNs 36445-71-3 and 70191-75-2. The robust summary for CASRN 36445-71-3 states that Benax 3B1 is similar to Dowfax 3B2 but it contains a different mix of alkyl chains (a mix of C-9 and C-10 linear chains). EPA agrees that the use of data for Benax 3B1 is appropriate.

1. Chemical Identity

1.1 Identification and Purity

The following description is taken from the final Test Plan (2002):

The ADPODS category consists of five ADPODS chemicals listed as HPV chemicals. Data for two additional ADPODS chemicals that have recently been subjected to more health and environmental studies have been added in summary to enrich the database on this category. Additionally, data from tests of the dry forms of two of the chemicals (the C6 and C16 members of the group) have also been included in order to more fully complete the data package. (These chemicals are normally sold as aqueous solutions and so have routinely been tested as such.) All of these ADPODS chemicals have a common Structure-Activity-Relationship [SAR] to serve as the technical basis for the category under the EPA HPV Challenge Program.

The structures of the ADPODS category members are shown in Table. 1.

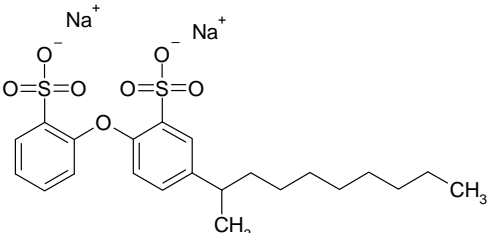
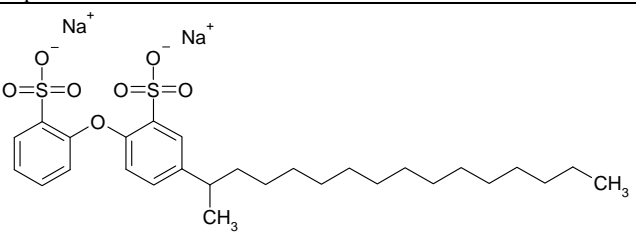
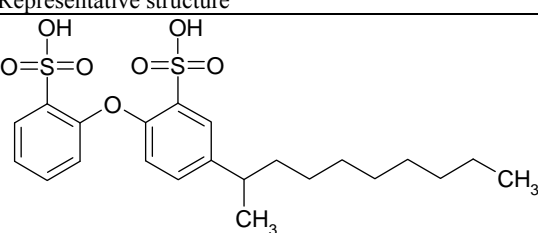
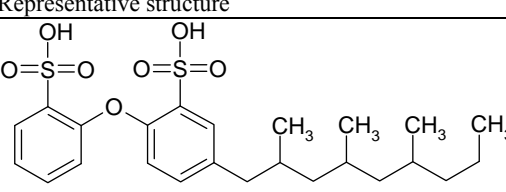
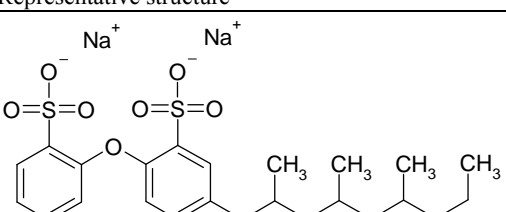
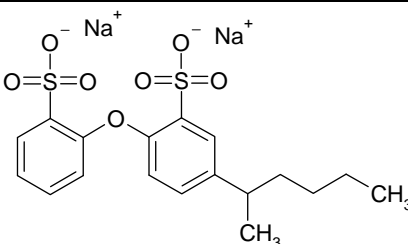
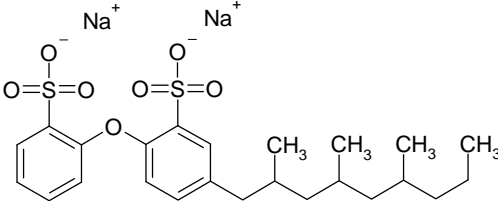
Table 1. Chemical Structure of Alkyl Diphenyl Oxide Disulfonates (ADPODS) Category Members		
Sponsored Chemicals		
Chemical Name	CASRN	Structure¹
Benzenesulfonic acid, decyl(sulfophenoxy)-, sodium salt (1:2)	36445-71-3	 <p style="text-align: center;">Representative structure</p>
Benzenesulfonic acid, hexadecyl(sulfophenoxy)-, sodium salt (1:2) ^{2,3}	65143-89-7	 <p style="text-align: center;">Representative structure</p>
Benzenesulfonic acid, decyl(sulfophenoxy)- ³	70191-75-2	 <p style="text-align: center;">Representative structure</p>
Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated ⁴	119345-03-8	 <p style="text-align: center;">Representative structure</p>
Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated, sodium salts ⁴	119345-04-9	 <p style="text-align: center;">Representative structure</p>

Table 1. Chemical Structure of Alkyl Diphenyl Oxide Disulfonates (ADPODS) Category Members

Sponsored Chemicals		
Chemical Name	CASRN	Structure ¹
Benzene, 1,1'-oxybis-, sec-hexyl derivs., sulfonated, sodium salts	147732-60-3	 <p>Representative structure</p>
Benzene, 1,1'-oxybis-, sec-dodecyl derivs., sulfonated, sodium salts ⁵	149119-20-0	 <p>Representative structure</p>

¹ The structures were drawn to the specifications presented in the test plan, where the sponsor states that the majority of the products are mono-alkylated and disulfonated. Several of the CAS names include the 'derivs.', which signifies that the substances are mixtures of compounds that are mono-alkylated, dialkylated, tri-alkylated, etc. 'Sulfonated' also designates that the substances can contain one or more sulfonic acid/salt groups.

² Benzenesulfonic acid, hexadecyl(sulfophenoxy)-, sodium salt (1:2) (CASRN 65143-89-7) is most likely produced using 1-hexadecene (CASRN 629-73-2), a commercially available compound.

³ Concerning alkylations on diphenyl ether rings, the sponsor states in the test plan (page 5) that what they describe as 'linear alkyls' are actually secondary alkyls in which the alkyl groups are attached to the phenyl rings at the second carbon of the alkyl chains. They describe the raw material for the alkylation as 'linear alkylate,' which presumably refers to linear alpha-olefins such as 1-hexene, 1-decene, etc. It is known that Friedel-Craft alkylations of aromatic rings, which employ 1-alkenes and either aluminum chloride or sulfuric acid as catalysts, preferentially yields the alkyl group attachment at the second carbon of the alkyl chain, followed by attachment at the third carbon of the chain. Little to no addition occurs at the first carbon of the alkyl chain. The addition of the 1-alkene to the ring follows the Markovnikov rule (as cited in Vora BV; et al. 1997. Kirk-Othmer Encyclopedia of Chemical Technology, Chapter on Alkylation. Vol. 10. John Wiley & Sons, Inc. Online Posting Date: February, 14, 2003).

⁴ The sponsor states that the branched C12 test substances are produced from tetrapropylene alkylate, presumably tetrapropylene containing a double bond at an unspecified position. This type of branched C12 alkyl group (CASRN 119345-04-9) is apparently also used to produce the substances sold in Europe under the CASRN's of 28519-02-0 and 25167-32-2, as indicated by the sponsor in the Test Plan (page 7). However, the CAS names for CASRN's 28519-02-0 and 25167-32-2 are benzenesulfonic acid, dodecyl(sulfophenoxy)-, sodium salt (1:2) and benzenesulfonic acid, oxybis[dodecyl]-, sodium salt (1:2), respectively, which indicates that the dodecyl group must be linear. A serious discrepancy therefore exists between the branched C12 substance sold in the US under the CASRN 119345-04-9, the description of the C12 substance sold in Europe, and the CAS names and numbers used for the C12 substance sold in Europe.

⁵ Benzene, 1,1'-oxybis-, sec-dodecyl derivs., sulfonated, sodium salts (CASRN 149119-20-0) is described by the sponsor as being a linear C12. The sponsor also comments that this chemical is listed under the CASRN 28519-02-0 for HPV purposes, whose name specifically denotes a linear C12 alkyl group. However, in the Test Plan (page 7), the sponsor notes that CASRN 28519-02-0, as sold in Europe, is actually a branched C12 alkyl group. Consequently, there is serious concern over whether CASRN 149119-20-0 is a linear or branched C12. It has been represented here as branched and based upon tetrapropylene.

1.2 Physical-Chemical Properties

The physical-chemical properties of the members of the ADPODS category are summarized in Table 1, while the environmental fate properties are provided in Table 2. The structures of the compounds are provided in the Appendix with a detailed discussion of several identity and chemical structure issues.

The alkyl diphenyl oxide sulfonates (ADPODS) are solid substances with negligible vapor pressure and are dispersible in water.

The physical-chemical properties of ADPODS category members are found in Table 2.

Table 2. Physical-Chemical Properties of the ADPODS Category¹

	SPONSORED CHEMICAL Benzenesulfonic acid, decyl(sulfophenoxy)-, sodium salt (1:2)	SPONSORED CHEMICAL Benzenesulfonic acid, hexadecyl(sulfophenoxy)-, sodium salt (1:2)	SPONSORED CHEMICAL Benzenesulfonic acid, decyl(sulfophenoxy)-	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated, sodium salts	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, sec-hexyl derivs., sulfonated, sodium salts	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, sec-dodecyl derivs., sulfonated, sodium salts
Property	Value	Value	Value	Value	Value	Value	Value
CASRN	36445-71-3	65143-89-7	70191-75-2	119345-03-8	119345-04-9	147732-60-3	149119-20-0
Molecular Weight	514.57	598.73	470.60	498.65	542.63	458.46	542.63
Physical State	Solid	Solid	Solid	Solid	Solid	Solid	Solid
Melting Point	No data	230°C (decomposition)	No data	No data	No data	330°C (decomposition)	No data
Boiling Point	>300°C (estimated) ²	Decomposes	>300°C (estimated) ²	>300°C (estimated) ²	>300°C (estimated) ²	Decomposes	>300°C (estimated) ²
Vapor Pressure	<1×10 ⁻¹⁰ mm Hg at 25°C (estimated) ²	<1×10 ⁻¹⁰ mm Hg at 25°C (estimated) ²	<1×10 ⁻¹⁰ mm Hg at 25°C (estimated) ²	<1×10 ⁻¹⁰ mm Hg at 25°C (estimated) ²	<1×10 ⁻¹⁰ mm Hg at 25°C (estimated) ²	<1×10 ⁻¹⁰ mm Hg at 25°C (estimated) ^{2,3}	<1×10 ⁻¹⁰ mm Hg at 25°C (estimated) ²
Water Solubility	Dispersible	Dispersible	Dispersible	Dispersible	Dispersible	Dispersible	Dispersible
Dissociation Constant (pK _a)	Not applicable	Not applicable	0.44 (estimated) ⁴	0.44 (estimated) ⁴	Not applicable	Not applicable	Not applicable

Table 2. Physical-Chemical Properties of the ADPODS Category¹

	SPONSORED CHEMICAL Benzenesulfonic acid, decyl(sulfophenoxy)-, sodium salt (1:2)	SPONSORED CHEMICAL Benzenesulfonic acid, hexadecyl(sulfophenoxy)-, sodium salt (1:2)	SPONSORED CHEMICAL Benzenesulfonic acid, decyl(sulfophenoxy)-	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated, sodium salts	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, sec-hexyl derivs., sulfonated, sodium salts	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, sec-dodecyl derivs., sulfonated, sodium salts
Property	Value	Value	Value	Value	Value	Value	Value
Henry's Law Constant	$<1 \times 10^{-10}$ atm-m ³ /mole (estimated) ²	$<1 \times 10^{-10}$ atm-m ³ /mole (estimated) ²	$<1 \times 10^{-10}$ atm-m ³ /mole (estimated) ²	$<1 \times 10^{-10}$ atm-m ³ /mole (estimated) ²	$<1 \times 10^{-10}$ atm-m ³ /mole (estimated) ²	$<1 \times 10^{-10}$ atm-m ³ /mole (estimated) ²	$<1 \times 10^{-10}$ atm-m ³ /mole (estimated) ²
Log K _{ow}	Not applicable due to dispersibility ⁵	Not applicable due to dispersibility ⁵	Not applicable due to dispersibility ⁵	Not applicable due to dispersibility ⁵	Not applicable due to dispersibility ⁵	Not applicable due to dispersibility ⁵	Not applicable due to dispersibility ⁵

¹The Dow Chemical Company. 2006. Revised Robust Summary and Test Plan for Alkyl Diphenyl Oxide Sulfonates (ADPODS). Available online at <http://www.epa.gov/chemrtk/pubs/summaries/adpods/c14165tc.htm> as of July 12, 2010.

²U.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/episuitedl.htm> as of July 12, 2010.

³A measured value of 0.0166 mm Hg at 25°C was reported for a commercial product named Dowfax XD-8292 (CASRN 147732-60-3); however, this vapor pressure is not likely to be accurate as this substance is a salt.

⁴SPARC. 2010. Online pK_a and Property Calculator, v.4.2.1405-s4.2.1408. Available online at <http://ibmlc2.chem.uga.edu/sparc/> as of July 20, 2010.

⁵Tolls J; Sijm D. 2000. Estimating properties of surface active chemicals. In: Handbook of Property Estimation for Chemicals. Boethling RS; Mackay D; eds. Chapter 17. Boca Raton, FL: Lewis Publishers pp. 419–446.

2. General Information on Exposure

2.1 Production Volume and Use Pattern

The ADPODS category chemicals had an aggregated production and/or import volume in the United States between 11.5 million pounds and 161 million pounds in calendar year 2005.

- CASRN 36445-71-3: 1 to <10 million pounds;
- CASRN 65143-89-7: 500,000 to <100 million pounds;
- CASRN 119345-03-8: < 500,000 pounds;
- CASRN 119345-04-9: 10 to <50 million pounds;
- CASRN 147732-60-3: < 500,000 pounds;

CASRN 70191-75-2 and 149119-20-0 were not reported in the 2006 IUR.

CASRN 36445-71-3:

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include soap and cleaning compound manufacturing as surface active agents. Non-confidential commercial and consumer uses of this chemical include soaps and detergents.

CASRN 65143-89-7:

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include soap and cleaning compound manufacturing as surface active agents and process regulators used in vulcanization or polymerization processes. Non-confidential commercial and consumer uses of this chemical include fabrics, textiles and apparel; and soaps and detergents.

CASRN 119345-03-8 and 147732-60-3:

No industrial processing and uses and commercial and consumer uses were reported.

CASRN 119345-04-9:

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include soap and cleaning compound manufacturing as process regulators used in vulcanization or polymerization processes. Non-confidential commercial and consumer uses of this chemical include fabrics, textiles and apparel; and paper products.

2.2 Environmental Exposure and Fate

The environmental fate properties are provided in Table 3.

The members of the ADPODS category are expected to have low mobility in soil. Several biodegradation studies using commercial products containing the members of the ADPODS category suggest that they are not readily biodegradable; however, they are unlikely to be highly persistent in the environment. Benzene, 1,1'-oxybis-, sec-hexyl derivs., sulfonated, sodium salts (CASRN 147732-60-3) was not degraded over the course of a 28-day incubation period using an activated sludge inoculum and the modified AFNOR test (OECD 301A). This compound

underwent 73% primary degradation in 21 days using a coupled units simulation test (OECD 303A), 79% degradation in 7 days using a semi-continuous activated sludge test (SCAS) (OECD 302A), and was classified as inherently degradable. In a non-GLP-compliant method benzene, 1,1'-oxybis-, sec-hexyl derivs., sulfonated, sodium salts reached 63.3% biodegradation after 19 days. A commercial product called Dowfax 8390 consisting of benzenesulfonic acid, hexadecyl(sulfophenoxy)-, sodium salt (1:2) (65143-89-7), achieved <6% biodegradation in 28 days using the closed bottle test (OECD 301D) and was classified as not readily biodegradable. It degraded 54% over 28 days using the modified Zahn-Wellens test (OECD 302B) and, while called inherently biodegradable by the submitter, did not meet the criteria (70% biodegradation) for inherent biodegradability for this test. A commercial product (Dowfax 3B2) consisting of benzenesulfonic acid, decyl(sulfophenoxy)-, sodium salt (1:2) (CASRN 36445-71-3), tested as a 45% solution of disodium mono- and didecylphenyloxide disulfonic acid in water achieved 0 and 4% DOC decrease in 28 days using an aerobic GLP-compliant Directive 84/449/EEC, C.4 method with an activated sludge inoculum. It only achieved 7.4% ultimate degradation within 28 days using a coupled units simulation test (OECD 303A); however, complete primary biodegradation was observed within 15 days. In an aerobic non-GLP-compliant EEC Directive 28/243/EEC and NF.T.73-265 test, benzenesulfonic acid, decyl(sulfophenoxy)-, sodium salt (1:2) achieved 75.4% biodegradation after 8 days and up to 92.2% biodegradation in 17 to 38 days. An aerobic GLP-compliant Soap and Detergent Association (SDA) SCAS method was used to determine the degree to which the biodegradation of Dowfax 3B2 would be reduced by the addition of another surfactant (Dowfax 2A1 - C12 branched sodium salt 45% in water). An apparent biodegradability of 98.7% for the Dowfax 3B2 substance alone was reported, which was reduced to 98.0, 95.9, and 90.8% with the addition of 4.5, 10, and 25% of the second surfactant (Dowfax 2A1), respectively.

In an aerobic GLP-compliant SDA's Subcommittee on Biodegradation Test method using activated domestic sludge inoculums, benzene, 1,1'-oxybis-, sec-dodecyl derivs., sulfonated, sodium salts (CASRN 149119-20-0) biodegraded by 99.6% after 23 hours. In modified Zahn-Wellens test (OECD 302B), benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated, sodium salts (CASRN 119345-04-9) degraded by 21% after 28 days as determined by loss of DOC, and 58% primary biodegradation was reached after 28 days as measured by HPLC analysis. The substance also degraded by 49% after 21 days in an OECD 'Confirmatory Test.' In an aerobic GLP-compliant SDA's Subcommittee on Biodegradation Test using activated domestic sludge, the observed apparent reduction in methylene blue active substance (MBAS) for Dowfax 2A1 (45% in water) was 51.0%.

Benzenesulfonic acid, hexadecyl(sulfophenoxy)-, sodium salt (1:2) CASRN 65143-89-7, tested as Dowfax 8390 (63.7% C16 linear sodium salt in water) degraded by 0–6% in 28 days by an aerobic GLP-compliant Directive 84/449/EEC, C.6 "Biotic degradation-closed bottle test" using a domestic activated sludge inoculum. It was inherently biodegradable by an aerobic GLP-compliant Directive 87/302/EEC Zahn-Wellens test. In an aerobic non-GLP-compliant SDA Confirming Test (SCAS) using a commercial product called XD 8390 (65143-89-7) with an acclimated activated sludge inoculum, the average biodegradation was 95.35% (pass) over 7 days. In subsurface soil, primary biodegradation of ¹⁴C-labeled linear monoalkylated (C16) disulfonated diphenyl oxide (MADS) occurred within 10–30 days while mineralization to ¹⁴CO₂ was <1% after 99 days. In surface sandy loam, primary biodegradation occurred within 4 days,

and after 85 days, mineralization was 12–29% of the initial radioactivity. The compound was not degraded in aquatic sediments under anaerobic conditions but showed ~89% primary biodegradation (partial degradation of the aliphatic side chain) of ^{14}C -MADS within 7 days in aerobic sediment. Mineralization to $^{14}\text{CO}_2$ reached 5% after 83 days and 15% after 181 days. In another test, little mineralization occurred using an acclimated activated sludge, while tests with activated sludge from a municipal waste water treatment plant showed primary biodegradation. In an aerobic non-GLP-compliant SCAS test using acclimated domestic sludge, the compound biodegraded by 95.84 and 94.47% over an average of 7 days.

Volatilization of the ADPODS category members is not expected to be an important environmental fate process since five of the compounds are salts, and the two acidic members are expected to exist as anions under environmental conditions. The rate of hydrolysis for the compounds in the ADPODS category is negligible. The members of the ADPODS category are expected to have moderate persistence (P2) and low bioaccumulation potential (B1) with the exception of benzenesulfonic acid, hexadecyl(sulfophenoxy)-, sodium salt (1:2), which may possess high bioaccumulation potential (B3).

Conclusions: The alkyl diphenyl oxide sulfonates (ADPODS) are solid substances with negligible vapor pressure and tend to be dispersible in water. The ADPODS are expected to have low mobility in soil. Volatilization of the ADPODS category members is not expected to be an important environmental fate process since many of the compounds are sodium salts and acid forms that will exist as anions under environmental conditions. The rate of hydrolysis is negligible for all category members. The rate of atmospheric photooxidation is moderate; however, these compounds are not expected to exist in the vapor phase. The members of the ADPODS category are expected to have moderate persistence (P2) and low bioaccumulation potential (B1) with the exception of benzenesulfonic acid, hexadecyl(sulfophenoxy)-, sodium salt (1:2), which may possess high bioaccumulation potential (B3).

Table 3. Environmental Fate Characteristics of the ADPODS Category¹

Property	SPONSORED CHEMICAL Benzenesulfonic acid, decyl(sulfophenoxy)-, sodium salt (1:2)	SPONSORED CHEMICAL Benzenesulfonic acid, hexadecyl(sulfo phenoxy)-, sodium salt (1:2)	SPONSORED CHEMICAL Benzenesulfonic acid, decyl(sulfophenoxy)-	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated, sodium salts	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, sec-hexyl derivs., sulfonated, sodium salts	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, sec-dodecyl derivs., sulfonated, sodium salts
	Value	Value	Value	Value	Value	Value	Value
CASRN	36445-71-3	65143-89-7	70191-75-2	119345-03-8	119345-04-9	147732-60-3	149119-20-0
Photodegradation Half-life	8.6 hours (estimated) ²	5.5 hours (estimated) ²	5.1 hours (estimated) ²	6.9 hours (estimated) ²	6.9 hours (estimated) ²	14 hours (estimated) ²	6.9 hours (estimated) ²
Hydrolysis Half-life	Stable	Stable	Stable	Stable	Stable	<6% degradation after 5 days; Stable (measured)	Stable
Biodegradation	0% after 28 days (not readily biodegradable); 4% after 28 days (not readily biodegradable); 7.4% after 13–50 days ; 75.4% after 8 days; 92.2% after 17–38 days; 77% after 19 days	0–6% after 28 days (not readily biodegradable); 54–99% after 7–28 days (inherently biodegradable)	No data	No data	21% after 21 days (inherently biodegradable); 49% after 21 days (not readily biodegradable); 51% after 21 days (not readily biodegradable)	0% after 28 days (not readily biodegradable) ; 73% MBAS removal after 21 days (not readily biodegradable) ; 63% after 19 days (not readily biodegradable) ; 79.2% after 7 days (not readily biodegradable)	99.6% after 23 hours (inherently biodegradable)

Table 3. Environmental Fate Characteristics of the ADPODS Category¹

Property	SPONSORED CHEMICAL Benzenesulfonic acid, decyl(sulfophenoxy)-, sodium salt (1:2)	SPONSORED CHEMICAL Benzenesulfonic acid, hexadecyl(sulfo phenoxy)-, sodium salt (1:2)	SPONSORED CHEMICAL Benzenesulfonic acid, decyl(sulfophenoxy)-	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, tetrapropylene derivs., sulfonated, sodium salts	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, sec-hexyl derivs., sulfonated, sodium salts	SPONSORED CHEMICAL Benzene, 1,1'-oxybis-, sec-dodecyl derivs., sulfonated, sodium salts
	Value	Value	Value	Value	Value	Value	Value
Bioaccumulation Factor	BAF = 247 (estimated) ²	BAF = 7235 (estimated) ²	BAF = 250 (estimated) ²	BAF = 399 (estimated) ²	BAF = 399 (estimated) ²	BAF = 10 (estimated) ²	BAF = 399 (estimated) ²
Log K _{oc}	5.5 (estimated) ²	7.1 (estimated) ²	5.5 (estimated) ²	5.9 (estimated) ²	5.9 (estimated) ²	4.4 (estimated) ²	5.9 (estimated) ²
Fugacity (Level III Model) ²	0.1	0.1	0.1	<0.1	<0.1	<0.1	<0.1
Air (%)	4.1	1.8	4.1	2.0	2.0	9.3	2.0
Water (%)	43.1	32.1	43.2	38.6	38.6	75.6	38.6
Soil (%)	52.6	66.0	52.6	59.3	59.3	15.1	59.3
Sediment (%)							
Persistence ³	P2 (moderate)	P2 (moderate)	P2 (moderate)	P2 (moderate)	P2 (moderate)	P2 (moderate)	P2 (moderate)
Bioaccumulation ³	B1 (low)	B3 (lhigh)	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B1 (low)

¹The Dow Chemical Company. 2006. Revised Robust Summary and Test Plan for Alkyl Diphenyl Oxide Sulfonates (ADPODS). Available online at <http://www.epa.gov/chemrtk/pubs/summaries/adpods/c14165tc.htm> as of July 12, 2010.

²U.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/episuitedl.htm> as of July 12, 2010.

³Federal 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

A summary of health effects data submitted for SIDS endpoints is provided in Table 4. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Oral Toxicity

C6 Linear, Sodium salt (CASRN 147732-60-3, supporting chemical)

(1) Fischer 344 male rats (3/dose) were administered C6 linear, Sodium salt via oral gavage at 1000 mg/kg (50% active ingredient in water) and observed for 14 days. No mortalities were observed.

LD₅₀ > 1000 mg/kg

(2) Fischer 344 male rats (3/dose) were administered C6 linear, Sodium salt via the oral route at 650, 1250 or 2500 mg/kg (50% active ingredient in water) and observed for 14 days. No mortalities were observed.

LD₅₀ > 2500 mg/kg

(3) Wistar rats (3/sex/dose) were administered C6 linear, Sodium salt via oral gavage in water at 2000 mg/kg and observed for 14 days. No mortalities were observed. No abnormalities were noted at necropsy.

LD₅₀ > 2000 mg/kg

C10 Linear, acid (CASRN 70191-75-2)

(1) Fischer 344 male rats (3/dose) were administered C12 linear, Sodium salt via oral gavage at 500 or 1000 mg/kg (50% active ingredient in water) and observed for up to 14 days. Mortality was observed at 1000 mg/kg.

LD₅₀ = 500 – 1000 mg/kg

(2) Sprague-Dawley female rats (6/dose) were administered C12 linear, Sodium salt via oral gavage at 315, 650, 1250 or 2500 mg/kg (50% active ingredient in water) and observed for up to 14 days. Mortality was observed at 2500 mg/kg.

LD₅₀ = 1505.5 mg/kg

C10 Linear, Sodium salt (CASRN 36445-71-3)

(1) Female Rats (3/dose; strain not specified) were administered C10 linear, Sodium salt via oral gavage at 0, 56.7, 113.4, 225, 450 or 900 mg/kg (45% active ingredient in water) in water and observed for up to 14 days. Mortality was observed at 900 mg/kg.

LD₅₀ = 900 mg/kg

(2) Sprague-Dawley female rats (6/dose) were administered C10 linear, Sodium salt via gavage at 315, 650, 1250, 2500 or 5000 mg/kg (50% active ingredient in water) and observed for 14 days. No information on mortality was provided. No treatment-related effects were observed upon gross pathological examination.

LD₅₀ = 1781 mg/kg

Benax 3B1, C9 and C10 linear, ADPODS Sodium salt (No CASRN identified, supporting chemical)

Male rats (5/dose; strain not specified) were administered Benax 3B1 via oral gavage at 0, 56.23, 112.47, 223.15, 446.3 or 892.6 mg/kg (44.63% active ingredient in water) in water and observed for up to 14 days. Mortality was observed at 892.6.

LD₅₀ = 633.75 mg/kg

C12 Linear, Sodium salt (CASRN 149119-20-0)

Fischer 344 male rats (3/dose) were administered C12 linear, Sodium salt via oral gavage at 1000 mg/kg (50% active ingredient in water) and observed for 14 days. No mortalities were observed.

LD₅₀ > 1000 mg/kg

C12 Branched, acid (CASRN 119345-03-8)

(1) Fischer 344 female rats (3/dose) were administered C12 branched, acid via oral gavage at 250 or 1000 mg/kg (50% active ingredient in water) and observed for up to 14 days. Mortality was observed at 1000 mg/kg.

LD₅₀ > 1000 mg/kg

(2) Female Rats (3/dose; strain not specified) were administered C12 branched, acid via oral gavage at 0, 252, 500, 1000, 2000 or 3980 mg/kg and observed for up to 14 days. Mortality was observed at the two highest doses.

LD₅₀ = 1000 – 2000 mg/kg

C12 Branched, Sodium salt (CASRN 119345-04-9)

(1) Fischer 344 female rats (3/dose) were administered C12 branched, Sodium salt via oral gavage at 1000 mg/kg (50% active ingredient in water) and observed for 14 days. No mortalities were observed.

LD₅₀ > 1000 mg/kg

(2) Female Sprague-Dawley rats (6/dose) were administered C12 branched, Sodium salt via oral gavage at 315, 650, 1250 or 2500 mg/kg (50% active ingredient in water) and observed for up to 14 days. Mortality was observed at the three highest-doses.

LD₅₀ = 988 mg/kg

C16 Linear, Sodium salt (CASRN 65143-89-7)

(1) Sprague-Dawley rats (5/sex) were administered C16 linear, Sodium salt in water via oral gavage at 5000 mg/kg and observed for 14 days. No mortality was observed. No treatment-related post-mortem observations were noted at termination of the study.

LD₅₀ > 5000 mg/kg

(2) Wistar rats (5/sex) were administered C16 linear, Sodium salt via oral gavage at 2500 mg/kg (50% active ingredient in water) and observed for 14 days. No mortality was observed. No treatment-related macroscopic abnormalities were observed at necropsy.

LD₅₀ > 2500 mg/kg

(3) Male Fischer 344 rats (3/dose) were administered C16 linear, Sodium salt via oral gavage at 1000 mg/kg (50% active ingredient in water) and observed for 14 days. No mortalities were observed.

LD₅₀ > 1000 mg/kg

(5) Female Sprague-Dawley rats (6/dose) were administered C16 linear, Sodium salt via oral gavage at 650, 1250, 2500, 3150, 4000 or 5000 mg/kg (50% active ingredient in water) and observed for 14 days. Mortality was noted in rats administered the two highest doses. Histopathological examination revealed slight, pale discoloration of the mucosal surface of the glandular portion of the stomach at 2500 mg/kg.

LD₅₀ = 3872 mg/kg

(6) Female Rats (3/dose) were administered C16 linear, Sodium salt via oral gavage at 126, 250, 500, 1000 or 1990 mg/kg (50% active ingredient in water) and observed for 14 days. No mortalities were observed. No treatment-related effects were observed at necropsy.

LD₅₀ > 1990 mg/kg

Acute Dermal Toxicity

C6 Linear, Sodium salt (CASRN 147732-60-3)

(1) Wistar rats (5/sex) were administered C6 linear, Sodium salt via the dermal route at 2000 mg/kg under occlusive conditions for 24 hours and observed for 14 days. No mortalities were observed.

LD₅₀ > 2000 mg/kg

(2) New Zealand white female rabbits (2/dose) were administered C6 linear, Sodium salt via the dermal route at 1000 mg/kg (50% active ingredient in water) under semi-occlusive conditions for 24 hours and observed 14 days. No mortalities were observed.

LD₅₀ > 1000 mg/kg

C10 Linear, Sodium salt (CASRN 36445-71-3)

(1) New Zealand white male rabbits (2/dose) were administered C10 linear, Sodium salt via the dermal route at 1000 mg/kg (50% active ingredient in water) under occlusive conditions (exposure duration not provided) and observed for 14 days. No mortalities were observed.

LD₅₀ > 1000 mg/kg

Benax 3B1, C9 and C10 linear, ADPODS Sodium salt (No CASRN identified, supporting chemical)

Rabbits (6/sex/dose; strain not identified) were administered Benax 3B1 via the dermal route at 220, 440 or 880 mg/kg (44% active ingredient in water) under occlusive conditions for 24 hours (observation period not specified). No mortalities were noted.

LD₅₀ > 880 mg/kg

C12 Linear, Sodium salt (CASRN 149119-20-0)

New Zealand white female rabbits (2/dose) were administered C12 linear, Sodium salt via the dermal route at 1000 mg/kg (50% active ingredient in water) under occlusive conditions for 24 hours and observed for 14 days. No mortalities were observed.

LD₅₀ > 1000 mg/kg

C12 Branched, Sodium salt (CASRN 119345-04-9)

New Zealand white male rabbits (2/dose) were administered C12 branched, Sodium salt via the dermal route at 1000 mg/kg (50% active ingredient in water) under occlusive conditions for 24 hours and observed for 14 days. No mortalities were observed.

LD₅₀ > 1000 mg/kg

C16 Linear, Sodium salt (CASRN 65143-89-7)

(1) Sprague-Dawley rats (5/sex) were administered C16 linear, Sodium salt via the dermal route at 2000 mg/kg under occlusive conditions for 24 hours and observed for 14 days. No mortalities were observed.

LD₅₀ > 2000 mg/kg

(2) Wistar rats (5/sex) were administered C16 linear Sodium salt via the dermal route at 1000 mg/kg (50% active ingredient in water) under occlusive conditions for 24 hours and observed for 14 days. No mortalities were observed.

LD₅₀ > 1000 mg/kg

Repeated-Dose Toxicity

C6 Linear, Sodium salt (CASRN 147732-60-3)

Sprague-Dawley CD rats (5/sex/dose) were administered C6 linear, Sodium salt Dowfax XD 8292 (45.8% active ingredient in water) via oral gavage at 0, 50, 250 or 1000 mg/kg/day for 28 days. Clinical signs of toxicity included post-dosing salivation among all animals at 1000 mg/kg/day. Minor changes in clinical chemistry (effects not specified) and urinalysis (effects not specified) were noted at 250 and 1000 mg/kg/day of both sexes. Histopathological examinations revealed acute inflammation of the glandular gastric mucosa at 250 mg/kg/day in females and 1000 mg/kg/day in both sexes. No mortalities were observed. No changes in food consumption, water consumption, body weights or food utilization were noted. No treatment-related effects for hematology, macroscopic examination or organ weights were detected.

LOAEL = 250 mg/kg/day (based on effects on clinical chemistry, urinalysis and histology)

NOAEL = 50 mg/kg/day

Benax 3B1, C9 and C10 linear, ADPODS Sodium salt (No CASRN, supporting chemical)

(1) Rats (10/sex/dose, strain not specified) were administered Benax 3B1 via the diet at 0 (control), 125, 250, 500 or 1000 mg/kg/day (50% active ingredient in water) for 92 days. At 1000 mg/kg/day, animals experienced decreased body weights, increased serum glutamate pyruvate transaminase (SGPT) activity, increased organ weights (organs not specified) and effects on histology (fatty liver and cloudy swelling in the kidneys).

LOAEL = 1000 mg/kg/day (based on effects on clinical chemistry, organ weights, body weight and histology)

NOAEL = 500 mg/kg/day

(2) Beagle dogs (2/sex/dose) were administered Benax 3B1 via continuous feed at 0 (control), 81, 163, and 279 mg/kg/day for males and 89, 177, and 325 mg/kg/day for females. Pre-exposure and 89-day hematology and clinical chemistries were obtained from all dogs. Growth depression and increased portal cellularity was seen in the livers of male rats at 279 mg/kg/day. Slight cloudy swelling of hepatic cells, were observed in the liver of female dogs at 325 mg/kg/day. Histopathological examinations showed no treatment related effects.

LOAEL (systemic toxicity)_{male} = 279 mg/kg/day (based on liver effects)

NOAEL (systemic toxicity)_{male} = 163 mg/kg/day

LOAEL (systemic toxicity)_{female} = 325 mg/kg/day (based on liver effects)

NOAEL (systemic toxicity)_{female} = 177 mg/kg/day

C12 Branched, Sodium salt (CASRN 119345-04-9)

(1) Rats (10/sex/dose; strain not identified) were administered C12 branched, sodium salt via the diet at 0, 0.01, 0.03, 0.1, 0.3 or 1% (~ 5, 14, 50, 150 or 500 mg/kg/day) for 90 days. Organ weight effects included an increase in the average weight of the liver and kidneys at 500 mg/kg/day in females. Histology revealed central lobular necrosis of the parenchymal cells, fatty degeneration, early but slight fibrosis and slight bile duct epithelium proliferation in the portal areas of the liver at 500 mg/kg/day in both sexes. At 500 mg/kg/day, growth retardation and mottled liver appearance was observed in female rats. No mortality or changes in body weight, food consumption, appearance or behavior were observed.

LOAEL (systemic toxicity) = 500 mg/kg/day (based on liver effects and growth retardation)

NOAEL (systemic toxicity) = 150 mg/kg/day

(2) Beagle dogs (2/sex/dose) were administered Benax 2A1 in the diet at 0 (control), 0.1, 0.3 and 1.0% (~ 40, 131 and 350 mg/kg/day) for 95 days. Decreased food consumption and decreased body weight gain in both sexes at 350 mg/kg/day was comparable to controls. Serum alkaline phosphatase (SAP) was increase at 350 mg/kg/day, however, no histopathological changes in the liver or liver/body weight ratios were significant.

LOAEL (systemic toxicity) = 350 mg/kg/day (based on decreased body weight gain and clinical chemistry)

NOAEL (systemic toxicity) = 131 mg/kg/day

(3) Beagle dogs (4/sex/dose) were administered via oral feed 0, 0.125, 0.25 and 0.5% Benax 2A1 (~ 0, 34, 65 and 128 mg/kg/day); (2 males and 4 females/dose) were administered 1.0% (~ 319 mg/kg/day) for two years. At 319 mg/kg/day, 2 males and 4 females showed growth retardation. One dog/sex at 319 mg/kg/day lost approximately 33.33% of their body weight and was sacrificed after 14 months of treatment. An increase in liver/body ratio was observed in the male dog sacrificed. Gastrointestinal irritation was observed also at this dose level for the first 45 days of dosing.

LOAEL (systemic toxicity) = 319 mg/kg/day (based on decreased growth and body weight gain, gastrointestinal irritation)

NOAEL (systemic toxicity) = 128 mg/kg/day

C16 Linear, Sodium salt (CASRN 65143-89-7)

(1) Sprague-Dawley rats (15/sex/dose) were administered C16 linear, sodium salt (37.6% active ingredient) via gavage at 0, 50, 100, 200 or 600 mg/kg/day for 90 days. Increased kidney weights were noted in females at the two highest doses and in males at the high-dose, histology revealed dilation of the renal tubules in high-dose females and clinical chemistry effects included increased serum glutamate pyruvate transaminase activity in males at all dose levels. No mortality or changes in body weight, hematology or urinalysis were observed.

LOAEL = 200 mg/kg/day (based on kidney effects)

NOAEL = 100 mg/kg/day

(2) Sprague-Dawley rats (number/dose) were administered C16 linear, sodium salt (36.7% active ingredient) via gavage at 0, 50, 250 or 1000 mg/kg/day for 28 days. Clinical signs of toxicity included salivation and loose feces among high-dose animals. Body weights decreased in high-dose males and absolute and relative liver and kidney weights were increased in high-dose females. Changes in clinical chemistry (effects not specified) and microscopic changes in the liver (effects not specified) were noted in high-dose animals. No mortality or changes in food consumption, water consumption, hematology or urinalysis were observed.

LOAEL = 1000 mg/kg/day (based on clinical chemistry changes and liver effects)

NOAEL = 250 mg/kg/day

(3) In a combined repeated-dose/reproductive/developmental toxicity study, CD rats (12/sex/dose) were administered C16 linear, sodium salt (Dowfax 8390, 37% active ingredient) via oral gavage at 0 (control), 25, 75, or 250 mg/kg/day for 7 days/week. Females were dosed once daily for two weeks prior to breeding, continuing through breeding (two weeks), gestation (3 weeks), lactation (4 days) and until necropsy (test day 50 or 54). Males were dosed once daily for two weeks prior to breeding and continuing through breeding (two weeks) up until the day of necropsy (test day 47). At 25 mg/kg/day, (1/12) males died and (2/12) females died at 75 mg/kg/day; the deaths were considered gavage errors. Respiratory difficulty was observed at all dose levels. At 75 mg/kg/day prothrombin times increased in males. At 250 mg/kg/day, mean alanine transaminase levels (both sexes) and mean aspartate transaminase (females) were significantly raised. Males showed a statistically significant decrease in total serum protein and bilirubinuria at 250 mg/kg/day. Histopathologic changes in the lungs corresponded to inflammation of the bronchi, bronchioles and alveoli in both sexes at all doses.

LOAEL (systemic toxicity) = 75 mg/kg/day (based on mortality)

NOAEL (systemic toxicity) = 25 mg/kg/day

(4) Beagle dogs (4/sex/dose) were administered C16 linear, sodium salt (37.6% active ingredient) in the diet at 0, 50, 100 or 200 mg/kg/day for 90 days to assess toxicological effects associated with daily ingestion. No mortalities were observed. A decrease in kidney and liver weights was observed in male and female rats at 200 mg/kg/day. The difference was not considered statistically significant. No treatment related effects were observed during histopathological examinations.

NOAEL = 200 mg/kg/day (highest dose tested)

Reproductive/Developmental Toxicity

C6 Linear, Sodium salt (CASRN 147732-60-3)

In a combined reproductive/developmental toxicity screening test, Sprague-Dawley rats (12/sex/dose) were administered, via gavage, 0, 125, 417 or 2083 mg/kg/day Dowfax C6 (43.4% active ingredient equivalent to 0, 60, 200 or 1000 mg/kg/day CASRN 147732-60-3) in distilled water from 2 weeks prior to mating for 42 days (males) or up to 54 days (females). Mortality and decreased mean body weights were observed at 1000 mg/kg/day in both sexes. Clinical signs of toxicity included decreased activity, salivation, soft and watery feces and audible and difficult breathing among high-dose males. Focal necrosis of the liver was noted in one animal that died. Developmental effects included decreased pup viability, activity and body weights in high-dose animals. No treatment-related systemic effects were noted for organ weights. No treatment-related reproductive or developmental effects were noted for external examination, estrous cycle length, number of estrous cycles, microscopic examination, organ weights, mating, fertility, fecundity indices, gestation length, gestation index, pup survival, stillborn index, total implantation scars, pup sex ratio or mean number of live pups/litter.

LOAEL (reproductive/developmental toxicity) = 1000 mg/kg/day (based on mortality, clinical signs of toxicity, body weight, histopathology and pup viability)

NOAEL (reproductive/developmental toxicity) = 200 mg/kg/day

C16 Linear, Sodium salt (CASRN 65143-89-7)

In a combined reproductive/developmental toxicity screening test, Sprague-Dawley rats (12/sex/dose) were administered C16 linear, Sodium salt via oral gavage at 0, 9.18, 27.53 or 91.75 mg/kg/day (36.7% active ingredient) from 2 weeks prior to mating for 47 days (males) or 50 – 54 days (females). Three deaths were noted, but were considered due to gavage complications. Clinical signs of toxicity included increased incidence of respiratory difficulties at all dose levels (considered due to aspiration of small amounts of surfactant material), clear perioral soiling, clear perinasal soiling, red perinasal soiling and decreased/soft feces. Changes in clinical chemistry included increased mean alanine transaminase activity (ALT) in high-dose males and females and increased mean aspartate transaminase (AST) in high-dose females. No effects on body weight, food consumption, functional tests or organ weights were observed. Additional effects on hematology, clinical chemistry, urinalysis and histology of the lungs were observed, but were not considered treatment-related. No reproductive or developmental effects were noted for gonadal function, mating behavior, conception, development of conceptus, parturition, litter size, pup survival, pup sex ratio, pup body weight, gross external abnormalities or early postnatal growth.

NOAEL (reproductive/developmental toxicity) = 91.75 mg/kg/day (highest dose tested)

(2) In a combined repeated-dose/reproductive/developmental toxicity study, described previously, CD rats (12/sex/dose) were administered C16 linear, sodium salt (Dowfax 8390, 37% active ingredient) via oral gavage at 0 (control), 25, 75, or 250 mg/kg/day for 7 days/week. Females were dosed once daily for two weeks prior to breeding, continuing through breeding (two weeks), gestation (3 weeks), lactation (4 days) and until necropsy (test day 50 or 54). Males were dosed once daily for two weeks prior to breeding and continuing through breeding (two weeks) up until the day of necropsy (test day 47). At 25 mg/kg/day, (1/12) males died and (2/12) females died at 75 mg/kg/day. Respiratory difficulty was observed at all dose levels. Body weight, reproductive indices, pup survival and sex ration were comparable to control values. There were no visible external morphologic alterations noted in offspring.

LOAEL (maternal toxicity) = 75 mg/kg/day (based on mortality)

NOAEL (maternal toxicity) = 25 mg/kg/day

NOAEL (reproductive/developmental toxicity) = 250 mg/kg/day (highest dose tested)

Genetic Toxicity – Gene Mutation

In vitro

C6 Linear, Sodium salt (CASRN 147732-60-3, supporting chemical)

(1) *Salmonella typhimurium* strains TA 98, TA100, TA1535 and TA1537 and *Escherichia coli* strain WP2uvrA were exposed to C6 linear, Sodium salt at concentrations of 0 (DMSO vehicle control), 50, 125, 250, 500, 1250 or 2500 µg/plate (50% active ingredient in water) in the presence and absence of metabolic activation. Positive controls were tested but their response was not provided. The cytotoxic concentration was 2500 µg/plate.

C6 Linear, Sodium salt was not mutagenic in this assay.

(2) *Salmonella typhimurium* strains TA98, TA100, TA 1535 and TA1537 and *Escherichia coli* strain WP2uvrA were exposed to C6 linear, Sodium salt at concentrations of 0 (physiological saline and DMSO solvent controls) and 6 – 10,000 µg/plate in the presence and absence of metabolic activation. Positive controls were used and produced an appropriate response. The cytotoxic concentration was 6800 – 10,000 µg/plate in the absence of metabolic activation and 10,000 µg/plate in the presence of metabolic activation.

C6 Linear, Sodium salt was not mutagenic in this assay.

C16 Linear, Sodium salt (CASRN 65143-89-7)

Salmonella typhimurium strains TA98, TA100, TA1535 and TA1537 were exposed to C16 linear, Sodium salt at 5 – 250 µg/plate (50% active ingredient in water) in the presence and absence of metabolic activation. Positive controls were used and produced an appropriate response. The cytotoxic concentration was 250µg/plate.

C16 Linear, Sodium salt was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vitro

C6 Linear, Sodium salt (CASRN 147732-60-3, supporting chemical)

(1) Rat lymphocytes were exposed to C6 linear, Sodium salt at 0, 25, 83.5 or 250 µg/mL in the absence of metabolic activation and 0, 83.5, 250 or 833.5 µg/mL (50% active ingredient in water) in the presence of metabolic activation. Positive controls were used and produced an appropriate response. The cytotoxic concentrations were 833.5 in the absence of metabolic activation and 250 – 833.5 in the presence of metabolic activation.

C6 Linear, Sodium salt did not induce chromosomal aberrations in this assay.

(2) Rat lymphocytes were exposed to C6 linear, Sodium salt at 0, 145.2, 290.4 or 387.2 µg/mL in the absence of metabolic activation and 0, 72.6, 290.4 or 774.4 µg/mL in the presence of metabolic activation. Positive controls were used and produced an appropriate response. The cytotoxic concentrations were 387.2 – 484 µg/mL in the absence of metabolic activation and 774.4 µg/mL in the presence of metabolic activation.

C6 Linear, Sodium salt did not induce chromosomal aberrations in this assay.

C16 Linear, Sodium salt (CASRN 65143-89-7)

(1) Cultured peripheral human lymphocytes were exposed to C16 linear, Sodium salt at 50, 166.5, 500 or 1665 µg/mL (50% active ingredient in water) in the presence and absence of metabolic activation. Positive controls were used and produced an appropriate response. The cytotoxic concentrations were 1000 µg/mL in the absence of metabolic activation and 3330 µg/mL in the presence of metabolic activation.

C16 Linear, Sodium salt did not induce chromosomal aberrations in this assay.

(2) Rat lymphocytes were exposed to C16 linear, Sodium salt at 0 (negative control), 16.7, 50, 75, 100, 150 or 166.7 µg/mL in the presence and absence of metabolic activation. Positive controls were used and produced an appropriate response. The cytotoxic concentration was 500 µg/mL.

C16 Linear, Sodium salt did not induce chromosomal aberrations in this assay.

(3) Chinese Hamster Ovary (CHO) cells were exposed to C16 linear, Sodium salt at 0 (negative control), 2.5 – 300 µg/mL. Positive controls were used and produced an appropriate response. The cytotoxic concentration was not provided.

C16 Linear, Sodium salt did not induce chromosomal aberrations in this assay.

In vivo

C16 Linear, Sodium salt (CASRN 65143-89-7)

Sprague-Dawley rats (5/sex/dose) were administered C16 linear, Sodium salt (36% aqueous solution dried to a powder containing 92.5% active ingredient) in oral feed at 0, 50, 100, 200 or 600 mg/kg-bw/day for 90 days. Bone marrow cells from all rats were processed to capture cells in metaphase. No chromosomal aberrations were observed. No information on the use or response of positive controls was provided.

C16 Linear, Sodium salt did not induce chromosomal aberrations in this assay.

Additional Information

Skin Irritation

C6 Linear, Sodium salt (CASRN 147732-60-3, supporting chemical)

Three rabbits were administered C6 linear, Sodium salt (0.5 g) to clipped skin under semi-occlusive conditions for 4 hours and assessed for up to 72 hours post-application. Exposure resulted in very slight to well-defined erythema with or without very slight edema.

C6 Linear, Sodium salt was slightly irritating to rabbit skin.

C10 Linear, Sodium salt (CASRN 36445-71-3)

Two rabbits were administered C10 linear, Sodium salt (dry powder or moistened with water, amount not specified) to intact abdominal skin for 5 consecutive days and abraded abdominal skin for 3 consecutive days under occlusive conditions. Redness (due to mechanical irritation) was observed in animals exposed to moistened C10 linear, Sodium salt.

C10 Linear, Sodium salt was not irritating to rabbit skin.

C12 Branched, Sodium salt (CASRN 119345-04-9)

Humans (25/sex) were administered C12 branched, Sodium salt (15% in water) (conditions and amount not specified). Fatiguing of the skin was observed.

C12 Branched, Sodium salt was not irritating to rabbit skin.

C16 Linear, Sodium salt (CASRN 65143-89-7)

(1) New Zealand White rabbits (nine/sex) were administered C16 linear, Sodium salt 0.05 mL, (10% active ingredient in water) on clipped skin with an occlusive dressing for 4 hours and observed for up to 7 days after treatment. The skin was wiped clean after exposure. There were no signs of dermal irritation.

C16 Linear, Sodium salt was not irritating to rabbit skin.

(2) New Zealand White rabbits (one female, two males) were administered C16 linear, Sodium salt (0.5 g) on clipped, intact skin with a semi-occlusive dressing for 4 hours and observed for 72 hours after treatment. The skin was wiped clean after exposure. Effects included very slight erythema and slight edema. The primary irritation index was 0.3.

C16 Linear, Sodium salt was slight irritating to rabbit skin.

(3) Three female New Zealand White rabbits were administered undiluted C16 linear, Sodium salt 0.25 mL, (50% active ingredient in water) on clipped skin with a semi-occlusive dressing for 4 hours and observed for 72 hours after treatment. The skin was wiped clean after exposure. Effects included slight, immediate erythema and edema.

C16 Linear, Sodium salt was slightly irritating to rabbit skin.

(5) New Zealand White rabbits (two males) were administered C16 linear, Sodium salt (dry and moistened with water, 0.5 g) to intact skin for five applications and abraded skin for three applications under occlusive conditions. Animals were observed until day 8. No irritation was seen under dry conditions. Under water-moistened conditions, slight erythema was observed and was considered due to mechanical injury.

C16 Linear, Sodium salt was slightly irritating to rabbit skin.

Eye Irritation

C6 Linear, Sodium salt (CASRN 147732-60-3, supporting chemical)

(1) Five percent aqueous C6 linear, Sodium salt 0.05 mL, (50% active ingredient in water) was instilled into the eyes of six rabbits. Observations were made at 24, 48 and 72 hours after administration. Slight conjunctival redness, slight chemosis, slight ocular discharge, reddened iris and corneal opacity were noted.

C6 Linear, Sodium salt was slightly irritating to rabbit eyes.

(2) Undiluted C6 linear, Sodium salt (33 mg) was instilled into the eyes of three rabbits. Observations were made at 1, 24, 48 and 72 hours and at 6, 7, 14 and 21 days after administration. Corneal injury including epithelial damage and neovascularization were observed. Other effects included iritic irritation and irritation of the conjunctivae consisting of redness, chemosis and discharge.

C6 Linear, Sodium salt was highly irritating to rabbit eyes.

C10 Linear, acid (CASRN 70191-75-2)

Undiluted C10 linear, acid (amount not specified) was instilled into both eyes of one rabbit. One eye was washed after 30 seconds while the other eye remained unwashed. Observations were made at 1, 24 and 48 hours and at 7 and 14 days. Slight discomfort, moderate to severe conjunctival redness and swelling, moderate reddening of the iris and moderate corneal injury were observed.

C10 Linear, acid was highly irritating to rabbit eyes.

C10 Linear, Sodium salt (CASRN 36445-71-3)

In three studies, undiluted C10 linear, Sodium salt 0.045 mL, (44.9% active ingredient in water) was instilled into the right eye of one male and five female New Zealand White rabbits. Observations were made at 1, 24, 48 and 72 hours and at 7, 14 and 21 days. Slight to marked redness, slight to moderate chemosis, slight to marked discharge, reddening of the iris and scattered or diffuse areas of opacity and/or slight opacity were observed on the corneas.

C10 Linear, Sodium salt was moderately irritating to rabbit eyes.

C12 Branched, acid (CASRN 119345-03-8)

(1) Undiluted 0.5 mL, (50% active ingredient in water) and diluted (0.005 mL, 5% solution in water) C12 branched, acid was instilled into both eyes of two rabbits. One eye of each rabbit was washed after 30 seconds and the other after 1 hour. Observations were made at 1, 24 and 48 hours and after 7 days. Instillation resulted in slight to extensive conjunctivitis, slight corneal damage and internal effects.

C12 Branched, acid was slightly irritating to rabbit eyes.

C12 Branched, Sodium salt (CASRN 119345-04-9)

(1) Diluted C12 branched, Sodium salt 0.005 mL, (5% active ingredient in water) was instilled into the conjunctival sac of the right eye of rabbits (three/sex). The eyes remained unwashed for 24 hours after dosing. Observations were made at 1, 24, 48 and 72 hours and at 7 days post-instillation. Slight or moderate conjunctival redness, slight or moderate ocular discharge, slight or moderate chemosis, slight or moderate chemosis and opacity of the cornea were observed.

C12 Branched, Sodium salt was moderately irritating to rabbit eyes.

(2) Undiluted C12 branched, Sodium salt 0.05 mL, (50% active ingredient in water) was instilled into both conjunctival sacs of 3 rabbits. One eye was washed after 30 seconds and the other after 1 hour. Observations were made at 24 and 48 hours and at 7, 14 and 21 days. Slight to moderate discomfort, moderate to severe conjunctival redness and swelling, discharge, very slight to moderate reddening of the iris and moderate corneal injury were observed.

C12 Branched, Sodium salt was highly irritating to rabbit eyes.

(3) C12 Branched, Sodium salt was instilled as a solid and at 0.01 and 0.001 mL dilutions (10 and 1% active ingredient in water, respectively) into the conjunctival sac of three rabbits. One eye of each rabbit was washed after 30 seconds and the other after 1 hour. Each animal received a different form of C12 branched, Sodium salt. Slight to marked pain, slight to moderate conjunctival irritation and corneal injury were observed.

C12 Branched, Sodium salt was irritating to rabbit eyes.

C16 Linear, Sodium salt (CASRN 65143-89-7)

(1) In five studies, C16 linear, Sodium salt (0.1 mL or 0.1 g) was instilled into the conjunctival sac of the male and female rabbits. The eyes remained unwashed or were washed after 30 seconds or 1 hour after dosing. Effects included slight to moderate conjunctival redness, slight to moderate chemosis, slight to moderate ocular discharge, slight to moderate conjunctival redness, corneal opacity and reddening of the iris. (Doses were provided as 5%, 100 or 50% active ingredient in water).

C16 Linear, Sodium salt was moderately irritating to rabbit eyes.

Skin Sensitization

C6 Linear, Sodium salt (CASRN 147732-60-3)

Dunkin-Hartley female guinea pigs (10/dose) were treated with C6 linear, Sodium salt. Intradermal induction consisted of two injections (0.1 mL per site) of the test material (1.0% w/v in water) with and without Freund's Complete Adjuvant (FCA), and a control with FCA, alone. After 1 week, animals were treated topically for 48 hours with 0.5 mL of a 50% dilution in water. Challenge consisted of a single, 24-hour, topical application (0.5 mL) at 50% w/v in water on one flank of each test and a control animal under an occlusive dressing. Observations were made at approximately 24 and 48 hours after removal of the dressing. The induction readings included severe erythema with cases of necrosis and small scabs. No edema or signs of skin reactions were evident after the challenge exposure.

C6 Linear, Sodium salt was not a dermal sensitizer in guinea pigs.

C16 Linear, Sodium salt (CASRN 65143-89-7)

(1) Guinea pigs (10) were exposed to C16 linear, Sodium salt at concentrations of 0.5% intracutaneous induction, 50% induction (not stated) and 50% occlusive epicutaneous challenged. Test animals were challenged on day 21 with 0.1 – 0.2 mL of a 2% solution (v/v in distilled water) to the skin under occlusive dressing for 24 hours. Dermal reactions were evaluated at 24 and 48 hours after the dressings were removed. One animal died of undetermined causes.

C16 Linear, Sodium salt was not a dermal sensitizer in guinea pigs.

(2) Guinea pigs (20) were exposed to C16 linear, Sodium salt (35% active ingredient in water). Induction was carried out with intradermal injections (0.1 mL) of Freund's Complete adjuvant in distilled water, 0.1% active ingredient (w/v) in distilled water and 0.1% active ingredient (w/v) in a preparation of FCA plus distilled water. A topical application (0.2 – 0.3 mL, 5% active ingredient v/v in distilled water) was applied under an occlusive dressing 1 week after intradermal injections. Challenge occurred on day 21 with 0.1 – 0.2 mL of a 2% solution (v/v in distilled water) applied to the skin under an occlusive dressing for 24 hours. Dermal reactions were evaluated at 24 and 48 hours after the dressings were removed. No skin sensitization was noted.

C16 Linear, Sodium salt was not a dermal sensitizer in guinea pigs.

(3) Guinea pigs (20) were exposed to C16 linear, Sodium salt (application amounts stated as percent of active ingredient). Induction consisted of 3 topical applications (0.5 mL) of 75% w/w concentrations of the test material in distilled water (or distilled water alone) on days 0, 7 and 14. Six-hour applications were on the same site under an occlusive dressing. Challenge on day 28 consisted of a single, 6-hour topical application (0.5 mL) at 75% w/w in distilled water under an occlusive dressing. Observations were made approximately 24 and 48 hours after removal of the patches. No adverse reactions were noted.

C16 Linear, Sodium salt was not a dermal sensitizer in guinea pigs.

(4) Male Hartley albino guinea pigs (10) received two dermal applications of 0.4 mL during a 3-week induction period. The concentration used for the third induction application was decreased to 50% in distilled water. Animals were challenged with 0.4 mL of 20% 2 weeks after the last induction application. Challenge caused slight erythema. (Test material was identified as 35% active ingredient in water.)

C16 Linear, Sodium salt was a dermal sensitizer in guinea pigs.

(5) Male Hartley albino guinea pigs (10) received two dermal applications of 0.1 mL of 2.9% C16 linear, Sodium salt (test material was a use dilution containing 2.9% (not specified)) in distilled water during a 3-week induction period. The concentration of C16 linear, Sodium salt was decreased to 1.5% following the second induction application. Animals were challenged with 0.4 mL of 1.5% C16 linear, Sodium salt 2 weeks after the last induction application. No adverse reactions were noted.

C16 Linear, Sodium salt was not a dermal sensitizer in guinea pigs.

(6) Female guinea pigs (20) were exposed to 0.5 mL of C16 linear, sodium salt by topical application to the same site on the scapula region during the induction phase. These induction applications were made on nine separate occasions during a 3-week period. Ten days after the last induction exposure, animals were challenged by 0.5 mL of C16 linear, sodium salt to the contralateral flank. A second challenge application was carried out 3 weeks after the first one.

C16 Linear, Sodium salt was a dermal sensitizer in guinea pigs.

Carcinogenicity

C12 Branched, Sodium salt (CASRN 119345-04-9)

Rats (30/sex/dose) were administered C12 branched, Sodium salt via oral feed at 0, 0.03, 0.1, 0.3 or 1.0% (~ 15, 50, 150 or 500 mg/kg/day) for 2 years.

C12 Branched, Sodium salt did not increase the incidence of tumors in this study.

Conclusion: The acute oral toxicity is low and the acute dermal toxicity is moderate in rats for all category members. In an oral repeated-dose toxicity study with CASRN 147732-60-3, inflammation of the glandular gastric mucosa was observed at 250 mg/kg/day; the NOAEL for systemic toxicity was 50 mg/kg/day. In a 92-day dietary repeated-dose toxicity study, the supporting chemical, C9 and C10 (Benax 3B1), showed increased serum glutamate pyruvate transaminase and organ weights, a decrease in body weights and reversible histological changes at 1000 mg/kg/day; the NOAEL for systemic toxicity was 500 mg/kg/day. In a 95-day dietary repeated-dose toxicity study in dogs, CASRN 36445-71-3 showed growth depression and increased portal cellularity in the liver of males at 279 mg/kg/day. Female dogs had slight cloudy swelling of the hepatic cells at 325 mg/kg/day. The NOAEL for systemic toxicity in dogs was 163 mg/kg/day (male) and 177 mg/kg/day (female). A 90-day dietary repeated-dose toxicity study in rats with CASRN 119345-04-9, showed central lobular necrosis of parenchymal cells and fatty degeneration in males at 500 mg/kg/day. At the same dose, females showed growth retardation with a statistically significant increase in average liver and kidney weights; the NOAEL for systemic toxicity was 150 mg/kg/day. In a 95-day repeated-dose toxicity study with CASRN 119345-04-9 in dogs, a decrease in body weight gain and clinical chemistry changes were seen at 350 mg/kg/day; the NOAEL for systemic toxicity was 131 mg/kg/day. In a two-year continuous feeding study with CASRN 119345-04-9 in dogs, a decrease in growth and body weight gain were observed at 319 mg/kg/day; the NOAEL for systemic toxicity was 128 mg/kg/day. A 90-day oral repeated-dose toxicity study in rats with CASRN 65143-89-7 showed a significant increase in kidney weights in females at 200 mg/kg/day and above; and in the males at 200 mg/kg/day; the NOAEL for systemic toxicity was 100 mg/kg/day. A combined repeated-dose/reproductive/developmental toxicity study in rats with CASRN 65143-89-7 showed mortality in male rats at 25 mg/kg/day and in females at 75 mg/kg/day. No treatment-related effects were observed on reproductive or developmental endpoints. The NOAEL for systemic toxicity was 25 mg/kg/day and the NOAEL for reproductive/developmental toxicity was 250 mg/kg/day (highest dose tested). A 90-day continuous feeding study with CASRN 65143-89-7 in dogs showed no treatment related effects; the NOAEL for systemic toxicity was 200 mg/kg/day (highest dose tested). In a combined reproductive/developmental toxicity screening test with CASRN 65143-89-7 in rats, no effects on reproductive or developmental parameters were observed; the NOAEL for reproductive/developmental toxicity was 91.75 mg/kg/day (highest dose tested). In a combined oral reproductive/developmental toxicity screening test with CASRN 147732-60-3 in rats, mortality was observed at 1000 mg/kg/day in both sexes; the NOAEL for systemic toxicity was 200 mg/kg/day. There were no treatment related effects on reproductive performance; the NOAEL for reproductive toxicity was 1000 mg/kg/day (highest dose tested). However, pup weights were significantly reduced at 1000 mg/kg/day; the NOAEL for developmental toxicity was 200 mg/kg/day. CASRN 147732-60-3 did not induce genetic mutations in bacteria *in vitro*. CASRN 147732-60-3 induced chromosomal aberrations in human lymphocytes but not in rat lymphocytes *in vitro*. CASRN

65143-89-7 did not induce genetic mutations in bacteria, human lymphocytes, rat lymphocytes or Chinese Hamster Ovary cells *in vitro*. CASRN 147732-60-3, 149119-20-0 and 119345-03-8 are irritating to the rabbit skin and eye. CASRN 36445-71-3 is irritating to the rabbit eye. CASRN 147732-60-3 is not a skin sensitizer in guinea pigs. CASRN 65143-89-7 is a skin and eye irritant in rabbits and not a skin sensitizer in guinea pigs. CASRN 119345-04-9 is irritating to the rabbit eye. CASRN 119345-04-9 did not show increased incidence of tumors in rats.

Table 4. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data

Endpoints	SPONSORED CHEMICAL C6 Linear, Na salt (147732-60-3)	SPONSORED CHEMICAL C10 Linear acid (70191-75-2)	SPONSORED CHEMICAL C10 Linear, Na salt (36445-71-3)	SUPPORTING CHEMICAL Benax 3B1 (No CASRN)	SPONSORED CHEMICAL C12 Linear, Na salt (149119-20-0)	SPONSORED CHEMICAL C12 Branched, acid (119345-03-8)	SPONSORED CHEMICAL C12 Branched, Na salt (119345-04-9)*	SPONSORED CHEMICAL C16 Linear, Na salt (65143-89-7)
Acute Oral Toxicity LD₅₀ (mg/kg-bw)	> 1000	500 – 900	900	633.75	> 1000	1000 – 2000	988	750
Acute Dermal Toxicity LD₅₀ (mg/kg-bw)	> 1000	No data > 1000 (RA)	> 1000	> 1000	> 1000	No data > 1000 (RA)	> 1000	> 1000
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg/day)	(rat) NOAEL = 50 LOAEL = 250	No data NOAEL = 50 LOAEL = 250 (RA)	No data NOAEL = 50 LOAEL = 250 (RA)	(rat) NOAEL = 500 LOAEL = 1000 (dog) NOAEL m/f = 279/325 LOAEL m/f = 163/177	No data NOAEL = 50 LOAEL = 250 (RA)	(dog; 95-day) NOAEL = 131 LOAEL = 350 (dog; 2 year) NOAEL = 128 LOAEL = 319	(rat) NOAEL = 150 LOAEL = 500	(rat; 90-day) NOAEL = 100 LOAEL = 200 (dog; 90-day) NOAEL = 200 (highest dose tested)
Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg/day) Reproductive Toxicity	(rat) NOAEL = 200 LOAEL = 1000	No data NOAEL = 200 LOAEL = 1000 (RA)	No data NOAEL = 200 LOAEL = 1000 (RA)	—	No data NOAEL = 200 LOAEL = 1000 (RA)	No data NOAEL = 200 LOAEL = 1000 (RA)	No data NOAEL = 200 LOAEL = 1000 (RA)	(rat) NOAEL = 250 (highest dose tested) (rat) NOAEL = 92 (highest dose tested)
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg/day) Maternal Toxicity	(rat) NOAEL = 200 LOAEL = 1000	No Data NOAEL = 200 LOAEL = 1000	No Data NOAEL = 200 LOAEL = 1000	—	No Data NOAEL = 200 LOAEL = 1000	No Data NOAEL = 200 LOAEL = 1000	No Data NOAEL = 200 LOAEL = 1000	(rat) NOAEL = 25 LOAEL = 75
Developmental Toxicity	NOAEL = 200 LOAEL = 1000	NOAEL = 200 LOAEL = 1000 (RA)	NOAEL = 200 LOAEL = 1000 (RA)		NOAEL = 200 LOAEL = 1000 (RA)	NOAEL = 200 LOAEL = 1000 (RA)	NOAEL = 200 LOAEL = 1000 (RA)	NOAEL = 250 (highest dose tested)

Table 4. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data

Endpoints	SPONSORED CHEMICAL C6 Linear, Na salt (147732-60-3)	SPONSORED CHEMICAL C10 Linear acid (70191-75-2)	SPONSORED CHEMICAL C10 Linear, Na salt (36445-71-3)	SUPPORTING CHEMICAL Benax 3B1 (No CASRN)	SPONSORED CHEMICAL C12 Linear, Na salt (149119-20-0)	SPONSORED CHEMICAL C12 Branched, acid (119345-03-8)	SPONSORED CHEMICAL C12 Branched, Na salt (119345-04-9)*	SPONSORED CHEMICAL C16 Linear, Na salt (65143-89-7)
Maternal Toxicity								(rat) NOAEL = 28 LOAEL = 92
Developmental Toxicity								NOAEL = 92 (highest dose tested)
Genetic Toxicity – Gene Mutation <i>In vitro</i>	Negative	No data Negative (RA)	No data Negative (RA)	—	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	Negative
Genetic Toxicity – Chromosomal Aberrations <i>In vitro</i>	Negative	No data Negative (RA)	No data Negative (RA)	—	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	Negative
Genetic Toxicity – Chromosomal Aberrations <i>In vivo</i>	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	—	No data Negative (RA)	No data Negative (RA)	No data Negative (RA)	Negative
Additional Information								
Skin Irritation	Slightly irritating	Highly irritating	Slightly irritating	Highly irritating	Not irritating	Moderately irritating	Moderately irritating	Highly irritating
Eye Irritation	Moderately irritating	Highly irritating	Highly irritating	Moderately irritating	Irritating	Moderately irritating	Highly irritating	Highly irritating
Sensitization	Not sensitizing	—	—	—	—	—	Not sensitizing	Sensitizing
Carcinogenicity	—	—	—	—	—	—	Negative (rat)	—

Measured data in bold text; (RA) = Read Across; — indicates that endpoint was not addressed for this substance; m = male; f = female

*There is an eighth substance included in the main list of category members on page 7/26 of the test plan (CASRN 28519-02-0), which is produced outside of the U.S. and appears to be a close analog of the C12 branched, Sodium salt compound (CASRN 119345-04-9).

4. Hazard to the Environment

A summary of aquatic toxicity data submitted is provided in Table 5. The table also indicates where data for tested category members are read-across (RA) to untested members of the category. The data for CASRN 147732-60-3 was not used for environmental hazard.

Acute Toxicity to Fish

C10 Linear Acid (CASRN 70191-75-2)

No data were submitted for this chemical.

C10 Linear, Na salt (CASRN 36445-71-3)

Fathead minnow (*Pimephales promelas*) were exposed to C10 linear, Na salt at nominal concentrations of 1.41, 1.88 or 2.50 mg/L (concentrations corrected for 50% active ingredient in water) under flow-through conditions for 96 hours. Measured concentrations were not provided.

96-h LC₅₀ = 1.83 mg/L

C12 Linear, Na salt (CASRN 149119-20-0)

Fathead minnow (*Pimephales promelas*) were exposed to C12 linear, Na salt at nominal concentrations of 0, 0.31, 0.48, 0.80, 1.22 or 1.84 mg/L (concentrations corrected for 50% active ingredient in water) under flow-through conditions for 96 hours. Measured concentrations were not provided. One hundred percent mortality was noted at ≥ 0.80 mg/L

96-h LC₅₀ = 0.47 mg/L

C12 Branched, Na salt (CASRN 119345-04-9)

(1) Fathead minnow (*Pimephales promelas*) were exposed to C12 branched, Na salt under flow-through conditions for 96 hours. Nominal and measured concentrations were not provided.

96-h LC₅₀ = 1.93 mg/L (concentration corrected for 50% active ingredient in water).

(2) Bluegill sunfish (*Lepomis macrochirus*) were exposed to C12 branched, Na salt under static conditions for 96 hours. Nominal and measured concentrations were not provided.

96-h LC₅₀ = 3.41 mg/L (concentration corrected for 50% active ingredient in water).

(3) Rainbow trout (*Salmo gairdneri*) were exposed to C12 branched, Na salt under static conditions for 96 hours. Nominal and measured concentrations were not provided.

96-h LC₅₀ = 2.33 mg/L (concentration corrected for 50% active ingredient in water).

Acute Toxicity to Aquatic Invertebrates

C12 Linear, Na salt (CASRN 149119-20-0)

Water fleas (*Daphnia magna*) were exposed to C12 linear, Na salt at nominal concentrations of 0, 0.17, 0.35, 0.68, 1.27 or 2.39 mg/L (concentrations corrected for 50% active ingredient in water) under flow-through conditions for 48 hours. Measured concentrations were not provided. Fifty-three percent mortality was noted at 2.39 mg/L.

48-h EC₅₀ = 2.3 mg/L

C16 Linear, Na salt (CASRN 65143-89-7)

Water fleas (*Daphnia magna*) were exposed to C16 linear, Na salt at nominal concentrations of 0.5, 0.9, 1.6, 2.8, 5, 9, 16 or 28 mg/L (concentrations corrected for 50% active ingredient in water) under static conditions for 48 hours. Measured concentrations were not provided.

48-h EC₅₀ = 6.95 mg/L

Toxicity to Aquatic Plants

C16 Linear, Na salt (CASRN 65143-89-7)

Green algae (*Pseudokirchneriella subcapitata*) were exposed to C16 linear, Na salt at nominal concentrations of 0, 10, 18, 32, 56 or 100 mg/L under static conditions for 72 hours. Measured concentrations were not provided.

72-h EC₅₀ (growth) > 100 mg/L

72-h EC₅₀ biomass = 42 mg/L (dry powder material)

Chronic Toxicity to Fish

C12 Linear, Na salt (CASRN 1149119-20-0)

Fathead minnow (*Pimephales promelas*) were exposed to C12 linear, Na salt at nominal concentrations of 0.0088, 0.0125, 0.0181, 0.0310, 0.0477 or 0.0758 mg/L (concentrations corrected for 50% active ingredient in water) under flow-through conditions for 32 days. Measured concentrations were not provided. No effects in the percent of hatched embryos, number of normal larvae at hatch, mean weight or mean length of survivors were noted. A reduction in larval survival was noted at ≥ 0.0181 mg/L.

NOEC = 0.0125 mg/L

MATC = 0.0125 – 0.0181 mg/L

Conclusion: The fish 96-h LC₅₀ for CASRN 36445-71-3 is 1.83 mg/L. The fish 96-h LC₅₀ for CASRN 149119-20-0 is 0.47 mg/L. The aquatic invertebrate 48-h EC₅₀ for CASRN 149119-20-0 is 2.3 mg/L. The 48-h aquatic invertebrate EC₅₀ value for CASRN 65143-89-7 is 6.95 mg/L. The toxicity to aquatic plants 72-h E_bC₅₀ for CASRN 65143-89-7 is 42 mg/L. The 32-d MATC chronic toxicity range for fish for CASRN 119345-03-8 is 0.0125-0.0181 mg/L.

Table 5. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Aquatic Toxicity Data						
Endpoints	SPONSORED CHEMICAL C10 Linear acid (70191-75-2)	SPONSORED CHEMICAL C10 Linear, Na salt (36445-71-3)	SPONSORED CHEMICAL C12 Linear, Na salt (149119-20-0)	SPONSORED CHEMICAL C12 Branched, acid (119345-03-8)	SPONSORED CHEMICAL C12 Branched, Na salt (119345-04-9)*	SPONSORED CHEMICAL C16 Linear, Na salt (65143-89-7)
Fish 96-h LC₅₀ (mg/L)	No Data 1.83 (RA)	1.83	0.47	No Data 0.47 (RA)	1.93	No data < 0.47 (RA)
Aquatic Invertebrates 48-h EC₅₀ (mg/L)	No Data 2.3 (RA)	No Data 2.3 (RA)	2.3	No Data 2.3 (RA)	No Data 2.3 (RA)	6.95
Aquatic Plants 72-h EC₅₀ (mg/L) (growth) (biomass)	No Data 42 (RA)	No Data 42 (RA)	No Data 42 (RA)	No Data 42 (RA)	No Data 42 (RA)	>100 42
Chronic Toxicity to Fish 32-day EC₅₀ (mg/L)	No Data MATC = 0.0125 – 0.0181 (RA)	No Data MATC = 0.0125 – 0.0181 (RA))	No Data MATC = 0.0125 – 0.0181 (RA)	MATC = 0.0125 – 0.0181	No Data MATC = 0.0125 – 0.0181 (RA)	No Data MATC = 0.0125 – 0.0181 (RA)

bold = measured data (i.e., derived from testing); (RA) = Read Across; — indicates that endpoint was not addressed for this substance.

*There is an eighth substance included in the main list of category members on page 7/26 of the test plan (CASRN 28519-02-0), which is produced outside of the U.S. and appears to be a close analog of the C12 branched, Na salt compound (CASRN 119345-04-9).