

SCREENING-LEVEL HAZARD CHARACTERIZATION Substituted Diphenylamines Category

**Benzenamine, 4-(1-methyl-1-phenylethyl)-N-4[4-(1-methyl-1-phenylethyl)phenyl]-
(CASRN 10081-67-1)**

Benzenamine, ar-nonyl-N-nonylphenyl (CASRN 36878-20-3)

Benzenamine, N-phenyl-, reaction products with 2,4,4-trimethylpentene (CASRN 68411-46-1)

Benzenamine, N-phenyl-, styrenated (CASRN 68442-68-2)

Benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives (CASRN 68608-77-5)

**Benzenamine, N-phenyl-, reaction products with styrene and 2,4,4-trimethylpentene
(CASRN 68921-45-9)**

**Benzenamine, N-phenyl- reaction products with 2,4,4-trimethylpentene and isobutylene
(CASRN 184378-08-3)**

The High Production Volume (HPV) Challenge Program¹ was conceived as a voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsored chemicals; sponsorship entailed the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data did not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to "SIDS" (Screening Information Data Set^{1,2}) endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment.

The Environmental Protection Agency's Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1400 sponsored chemicals by developing hazard characterizations (HCs). These HCs consist of an evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. They are not intended to be definitive statements regarding the possibility of unreasonable risk of injury to health or the environment.

The evaluation is performed according to established EPA guidance^{2,3} and is based primarily on hazard data provided by sponsors; however, in preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor's responses to comments and revisions made to the submission. In order to determine whether any new hazard information was developed since the time of the HPV submission, a search of the following databases was made from one year prior to the date of the HPV Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, EXTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS,

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>.

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.

Chemical Abstract Service Registry Number (CASRN)	<p>10081-67-1 36878-20-3 68411-46-1 68442-68-2 68608-77-5 68921-45-9 184378-08-3</p>
Chemical Abstract Index Name	<p>Benzeneamine, 4-(1-methyl-1-phenylethyl)-N-4[4-(1-methyl-1-phenylethyl) phenyl]- Benzeneamine, AR-nonyl-N-(nonylphenyl)- Benzeneamine, N-phenyl-, reaction products with 2,4,4-trimethylpentene Benzeneamine, N-phenyl-, styrenated Benzeneamine, 2-ethyl-N-(2-ethylphenyl)-(tripropynyl) derivatives N-phenyl-, reaction products with styrene and 2,4,4-trimethylpentene Benzeneamine, N-phenyl- with 2,4,4-trimethylpentene and isobutene</p>
Structural Formula	See Section 1

Summary

Substituted diphenylamines are solids and viscous liquids with negligible to low water solubility, except for the supporting chemical, Diphenylamine(CASRN 122-39-4) which has moderate water solubility. Substituted diphenylamines have negligible to moderate vapor pressures. They are expected to have low mobility in soil. Volatilization of most members of substituted diphenylamines from water and moist soil is considered low-to-moderate based on their estimated Henry's Law constant, except for CASRN 10081-67-1, CASRN 68442-68-2 and CASRN 68921-45-9 which are expected to volatilize slowly. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered rapid. Persistence of substituted diphenylamines is expected to range from low to high (P1 to P3). The bioaccumulation potential for the category members also ranges from low (B1) to high (B3).

The acute oral toxicity of category members CASRN 68442-68-2, 184378-08-3, 101-67-7 and 68608-77-5 in rats is low, and the acute dermal toxicity of three of them (CASRN 68442-68-2, 101-67-7 and 68608-77-5) in rabbits is also low. A combined repeated-dose/ reproductive/ developmental toxicity study by the oral route in rats with category member CASRN 184378-08-3 showed hematological and hepatic toxicity at 125 mg/kg/day in males and hepatic toxicity at 25 mg/kg/day in females; the NOAEL for systemic toxicity for male rats was 25 mg/kg/day; the NOAEL for systemic and maternal toxicity for female rats was 5 mg/kg/day. In the same study, there was reproductive toxicity at 125 mg/kg/day as demonstrated by shorter gestations lengths and lower viability indices; the NOAEL for reproductive toxicity was 25 mg/kg/day. There was evidence of developmental toxicity in this study as demonstrated by decreases in offspring viability and body weights at 125 mg/kg/day; the NOAEL for developmental toxicity was 25 mg/kg/day. A repeated-dose toxicity study by the oral route in rats with CASRN 68921-45-9

showed decreased body weights and liver toxicity at 125 mg/kg/day, the lowest dose, the NOAEL for systemic toxicity is not established. An oral combined repeated-dose/reproductive/developmental toxicity screening study in rats with category member 68442-68-2 showed increased liver and adrenal weights and toxicity of the liver and thyroid glands-at 600 mg/kg/day; the NOAEL for systemic and maternal toxicity was 250 mg/kg-bw/day. In the same study, there was reproductive toxicity at 600 mg/kg/day as demonstrated by higher pre-implantation losses; the NOAEL for reproductive toxicity was 250 mg/kg/day. There was evidence of developmental toxicity as demonstrated by diminished surface righting at 600 mg/kg-bw/day; the NOAEL for developmental toxicity was 250 mg/kg/day. Category members did not induce gene mutations or chromosomal aberrations when tested *in vitro* or *in vivo*. Category member CASRN 68442-68-2 is slightly irritating to both the eyes and skin; category members CASRN 101-67-7 and 68608-77-5 are slightly irritating to the eyes. Skin irritation was not observed with category members CASRN 68921-45-9 and 101-67-7. Category members CASRN 68921-45-9 and 184378-08-3 are not dermal sensitizers.

The measured acute toxicity values of substituted diphenylamines to fish aquatic invertebrate and aquatic plants have no effects at the saturation limit (4.2×10^{-7} mg/L).

No data gaps were identified in the HPV Challenge Program.

The sponsor, the American Chemistry Council, Rubber and Plastic Additives (RAPA) Panel, submitted a Test Plan and Robust Summaries to EPA for the Substituted Diphenylamines Category on December 18, 2001. EPA posted the submission on the ChemRTK HPV Challenge website on January 15, 2002

(<http://www.epa.gov/chemrtk/pubs/summaries/subdipha/c13378tc.htm>). EPA comments on the original submission were posted to the website on December 3, 2002. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on August 25, 2003 and November 17, 2006, which were posted to the ChemRTK website on October 24, 2003 and January 19, 2007 respectively. The substituted diphenylamines category consists of 7 chemicals as shown in Table 1.

Category Justification

The eight members of the substituted diphenylamines category are diphenylamines with various degrees of phenyl or alkyl substitution; some of which are complex mixtures, also called Class 2 substances. Class 2 substances are composed of several chemicals whose concentration is variable depending on the degree of their synthesis. All substances in the category share a common starting material, diphenylamine (benzenamine, N-phenyl-; CASRN 122-39-4) and a common synthetic pathway. The sponsor grouped the chemicals into one category based on the similarities in structure, physical-chemical and environmental fate properties and aquatic and mammalian toxicities. EPA has arrayed the category chemicals roughly according to trends in the submitted physical-chemical properties, because they are expected to correlate with toxicity.

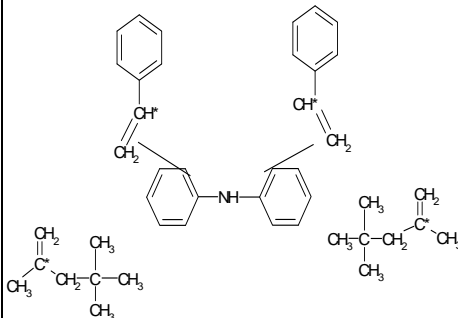
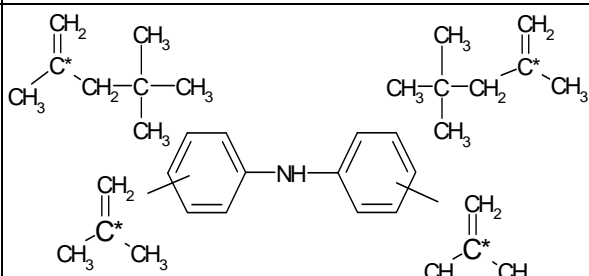
1 Chemical Identity

1.1 Identification and Purity

The following description is taken from the final Test Plan (2003):

All of these chemicals share a common starting material; Diphenylamine (Benzenamine, N-phenyl-, CAS# 122-39-4), a common synthetic pathway, and all compounds in this category are diamines with various substitutions. The chemical structures of these chemicals in this category are listed in Table 1.

Table 1. Chemical structures of Substituted Diphenylamines		
Chemical Name	CASRN	Structure
Benzenamine, 4-octyl- <i>N</i> -(4-octylphenyl)	101-67-7	
Benzenamine, 4-(1-methyl-1-phenylethyl)- <i>N</i> -4[4-(1-methyl-1-phenylethyl)phenyl]phenyl]-	10081-67-1	
Benzenamine, ar-nonyl- <i>N</i> -nonylphenyl	36878-20-3	
Benzenamine, <i>N</i> -phenyl-, reaction products with 2,4,4-trimethylpentene	68411-46-1	<p>According to the Test Plan attachment occurs at the * Carbon</p>
Benzenamine, <i>N</i> -phenyl-, styrenated	68442-68-2	
Benzenamine, 2-ethyl- <i>N</i> -(2-ethylphenyl)-, (tripropenyl) derivatives	68608-77-5	

Table 1. Chemical structures of Substituted Dipenylamines		
Chemical Name	CASRN	Structure
Benzenamine, <i>N</i> -phenyl-, reaction products with styrene and 2,4,4- trimethylpentene	68921-45-9	 <p>According to the Test Plan attachment occurs at the * Carbon</p>
Benzenamine, <i>N</i> -phenyl- reaction products with 2,4,4-trimethylpentene and isobutylene	184378-08-3	 <p>According to the Test Plan attachment occurs at the * Carbon</p>

1.2 Physical-Chemical Properties

The physical-chemical properties of the substituted dipenylamines category are summarized in Table 2. Substituted dipenylamines are solids and viscous liquids with negligible to low water solubility, except for the supporting chemical, diphenylamine (CASRN 122-39-4) which has moderate water solubility. Substituted dipenylamines have negligible to moderate vapor pressures.

Table 2. Physical-chemical Properties of Substituted Diphenylamines Category¹

Property	Benzenamine, 4-octyl- <i>N</i> -(4-octyl-phenyl)-	Benzenamine, 4-(1-methyl-1-phenylethyl)- <i>N</i> -[4-(1-methyl-1-phenylethyl)-phenyl]-	Benzenamine, ar-nonyl- <i>N</i> -(nonyl-phenyl)-	Benzenamine, <i>N</i> -phenyl-, reaction products with 2,4,4-trimethyl-pentene	Benzenamine, <i>N</i> -phenyl-, styrenated	Benzenamine, 2-ethyl- <i>N</i> -(2-ethyl-phenyl)-, (tri-propenyl) derivs.	Benzenamine, <i>N</i> -phenyl-, reaction products with styrene and 2,4,4-trimethyl-pentene	Benzenamine, <i>N</i> -phenyl-, reaction products with isobutylene and 2,4,4-trimethyl-pentene	Diphenyl-amine (Supporting Chemical)
CASRN	101-67-7	10081-67-1	36878-20-3	68411-46-1	68442-68-2	68608-77-5	68921-45-9	184378-08-3	122-39-4
Molecular Weight	393.72 ²	406	422	298–350	320	225–479	225–633	225–393	169
Physical State	Solid ²	Solid	Thick liquid	Liquid ³	Liquid	Liquid	Liquid	Solid/ Viscous liquid	Solid
Melting Point	87–95°C (measured) ²	98.5°C (measured)	<0°C (estimated)	<20°C (estimated); ³	~6°C (measured)	<0°C (estimated)	<0°C (estimated)	10°C (measured pour point)	52.5–55.5°C (measured) ⁴
Boiling Point	200°C at 0.5 mm Hg (measured) ² extrapolated to 419°C at 760 mm Hg ⁶	507°C (estimated) ⁵	258°C at 375 mm Hg (measured) extrapolated to 285°C at 760 mm Hg ⁶ ; Decomposes around 260°C at 760 mm Hg	362°C (estimated for lowest weight material) ²	>300°C (estimated); 393 °C (estimated for lowest weight material) ⁵	221°C (measured); 520°C (estimated for lowest weight material) ⁵	>198°C (measured); 175°C (measured);	Decomposes at 275°C; 302 to >360 (estimated)	~159°C at 91.5 mm Hg ⁴ ; ~261°C at 300 mm Hg ⁴ ; 302°C at 760 mm Hg (measured) ⁴
Vapor Pressure	2.3×10 ⁻⁷ mm Hg at 25°C (estimated from reduced boiling point) ⁶	3.5×10 ⁻⁹ mm Hg (estimate) ⁵	0.003 mm Hg at 25 °C (estimated from reduced boiling point) ⁶	2×10 ⁻⁵ mm Hg at 25°C ² ; 8.6×10 ⁻⁵ –3.8×10 ⁻⁸ mm Hg (estimated) ²	1.25×10 ⁻⁵ (estimated) ⁵	1.8×10 ⁻⁸ –6.9×10 ⁻¹² mm Hg at 25°C (estimated) ²	7.5×10 ⁻⁷ –1.4×10 ⁻¹⁵ mm Hg (estimated)	7.1×10 ⁻⁷ mm Hg at 25°C (measured); 8.56×10 ⁻⁵ –3.79×10 ⁻⁸ mm Hg (estimated)	1.61×10 ⁻⁴ mm Hg at 20°C ⁴ (measured); 0.98 mm Hg at 108°C ⁴
Dissociation Constant (pK _a)	1.97 (estimated) ⁷	1.32 (estimated) ⁷	0.95–1.61 (estimated for mono- and di-substitutions) ⁷	1.25–1.43 (estimated) ⁷	1.32 (estimated) ⁷	1.28 (estimated) ⁷	0.48–0.77 (estimated) ⁷	1.25–1.43 (estimated) ⁷	0.78 (measured) ⁸

Property	Benzenamine, 4-octyl- <i>N</i> -(4-octyl-phenyl)-	Benzenamine, 4-(1-methyl-1-phenylethyl)- <i>N</i> -[4-(1-methyl-1-phenylethyl)-phenyl]-	Benzenamine, ar-nonyl- <i>N</i> -(nonyl-phenyl)-	Benzenamine, <i>N</i> -phenyl-, reaction products with 2,4,4-trimethyl-pentene	Benzenamine, <i>N</i> -phenyl-, styrenated	Benzenamine, 2-ethyl- <i>N</i> -(2-ethyl-phenyl)-, (tri-propenyl) derivs.	Benzenamine, <i>N</i> -phenyl-, reaction products with styrene and 2,4,4-trimethyl-pentene	Benzenamine, <i>N</i> -phenyl-, reaction products with isobutylene and 2,4,4-trimethyl-pentene	Diphenyl-amine (Supporting Chemical)
CASRN	101-67-7	10081-67-1	36878-20-3	68411-46-1	68442-68-2	68608-77-5	68921-45-9	184378-08-3	122-39-4
Henry's Law Constant	6.676×10^{-5} atm-m ³ /mole (estimated) ²	2.6×10^{-8} atm-m ³ /mole (estimated) ⁵	1.12×10^{-5} – 1.2×10^{-4} atm-m ³ /mole (estimated for mono- and di-substitutions) ⁵	8.42×10^{-6} atm-m ³ /mole (estimated) ⁵	1.47×10^{-8} – 1.24×10^{-7} atm-m ³ /mole (estimated for mono- and di-styryl components) ⁵	2.4×10^{-5} – 2.56×10^{-4} atm-m ³ /mole (estimated for mono- and di-substitutions) ⁵	5.54×10^{-10} – 2.41×10^{-8} atm-m ³ /mole (estimated for mono- and di-substitutions) ⁵	5.23×10^{-5} – 7.4×10^{-6} atm-m ³ /mole (estimated for mono- and di-substitutions) ⁵	2.82×10^{-6} atm-m ³ /mole (estimated) ⁵
Water Solubility	4.215×10^{-7} mg/L (estimated) ²	1.5×10^{-4} (estimate) ⁵	1.7×10^{-7} mg/L (estimate) ⁵	0.015 mg/L (estimated for lowest weight material) ⁵	0.41 mg/L at 20°C (measured); 20.6 µg/L (measured for p-SDPA); <58.8 µg/L (measured for p,p'-diSDPA); <27.6 µg/L (measured for o,p,p'-triSDPA)	2.3×10^{-5} to 5.8×10^{-10} mg/L (estimated) (insoluble)	Negligible; 0.39 to 1.9×10^{-11} mg/L at 25°C (estimated)	0.0909– 5.93×10^{-5} mg/L at 20°C (measured); 1.167– 1.939×10^{-6} mg/L (estimated)	40 mg/L at 25°C ⁴ (measured); ~50 mg /L at 25°C ⁴
Log K _{ow}	11.26 (estimated) ²	8.51 (estimated) ⁵	12.24 (estimated) ⁵	>6 (measured) ² ; 7.05 (estimated, lowest weight material) ⁵	4.64 at 22°C (measured)	9.84 (estimated)	5.2 (measured); 5.45–15.13 (estimated)	3.13 to >6.2 (measured); 5.2–10.82 (estimated)	3.5 (measured) ⁴ ; 3.6 (estimated) ⁴

Table 2. Physical-chemical Properties of Substituted Diphenylamines Category¹

Property	Benzenamine, 4-(1-methyl-1-phenylethyl)- <i>N</i> -[4-(1-methyl-1-phenylethyl)phenyl]-	Benzenamine, 4-(1-methyl-1-phenylethyl)- <i>N</i> -[4-(1-methyl-1-phenylethyl)phenyl]-	Benzenamine, ar-nonyl- <i>N</i> -(nonyl-phenyl)-	Benzenamine, <i>N</i> -phenyl-, reaction products with 2,4,4-trimethyl-pentene	Benzenamine, <i>N</i> -phenyl-, styrenated	Benzenamine, 2-ethyl- <i>N</i> -(2-ethyl-phenyl)-, (tri-propenyl) derivs.	Benzenamine, <i>N</i> -phenyl-, reaction products with styrene and 2,4,4-trimethyl-pentene	Benzenamine, <i>N</i> -phenyl-, reaction products with isobutylene and 2,4,4-trimethyl-pentene	Diphenyl-amine (Supporting Chemical)
CASRN	101-67-7	10081-67-1	36878-20-3	68411-46-1	68442-68-2	68608-77-5	68921-45-9	184378-08-3	122-39-4

¹The Rubber and Plastic Additive Panel. December 21, 2006. Revised Robust Summary and Test Plan for Substituted Diphenylamine Category.

<http://www.epa.gov/chemrtk/pubs/summaries/subdipha/c13378tc.htm>.

²The Rubber and Plastic Additive Panel. August 2003. Revised Robust Summary for Substituted Diphenylamine Category.

<http://www.epa.gov/hpv/pubs/summaries/subdipha/c13378rr.pdf>.

³The sponsor indicated that major components of the reaction melt at 44-107°C. However, the sponsor reported that it is a liquid at standard conditions.

⁴The Rubber and Plastic Additive Panel. December 2001. Robust Summary and Test Plan for Substituted Diphenylamine Category.

<http://www.epa.gov/hpv/pubs/summaries/subdipha/c13378tc.htm>.

⁵U.S. EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v 3.20. United States Environmental Protection Agency, Washington, DC, USA. <http://www.epa.gov/opptintr/exposure/pubs/episuite.htm>.

⁶NOMO5, 1987. Programs to Enhance PC-GEMS Estimates of Physical Properties for Organic Compounds. The Mitre Corp.

⁷SPARC. 2008. Online pK_a and Property Calculator v. 4.2.1405-s4.2.1408. Accessed September 7, 2008.

<http://ibmlc2.chem.uga.edu/sparc/index.cfm?CFID=32727&CFTOKEN=65477992>.

⁸SRC. The Physical Properties Database (PHYSPROP). Syracuse, NY: Syracuse Research Corporation. Available from <http://www.syrres.com/esc/physprop.htm> as of September 25, 2008.

*In some instances it could not be determined whether a value was estimated or measured. The original Test Plan included Benzenamine, 4-(1,1,3,3-tetramethylbutyl)-*N*-[4-(1,1,3,3-tetramethylbutyl)phenyl]- (CASRN 15721-78-5); however, this compound was removed in the subsequent revisions and is no longer sponsored by the Rubber and Plastic Additive Panel.

2 General Information on Exposure

2.1 Production Volume and Use Pattern

This category has an aggregated production and/or import volume in the United States of 22 million to 112.5 million pounds. This aggregated production volume does not include CASRN 10081-67-1 and 184378-08-3 which did not have IUR reports. The volumes for the category members were:

CASRN 101-67-7	<500,000 pounds
CASRN 68442-68-2	500,000 to 1 million pounds
CASRN 68608-77-5	500,000 to 1 million pounds
CASRN 68921-45-9	1 million to 10 million pounds
CASRN 36878-20-3	10 million to 50 million pounds
CASRN 68411-46-1	10 million to 50 million pounds
CASRN 184378-08-3	No 2006 IUR data
CASRN 10081-67-1	No 2006 IUR data

Non-confidential IUR information indicates that the industrial processing and uses of these chemicals include stabilizers, lubricants and reactants. Non-confidential information in the IUR indicates that the commercial and consumer products containing the chemicals include lubricants, greases and fuel additives. The HPV submission for this category states that these chemicals are used as antidegradants in rubber, foamed polymers and high-temperature fluids, such as lubricants, gear oils, and hydraulic fluids. The HSDB information for CASRN 101-67-7 states that the chemical is used as an antioxidant for rubbers, plastics, and petroleum-based & synthetic lubricants.

2.2 Environmental Exposure and Fate

No quantitative information is available on releases of these chemicals to the environment. Based on EPA experience with the new chemicals program, there is generally a low potential for environmental releases to water for lubricants, greases and fuel.

The environmental fate properties of the category chemicals are provided in Table 3. Substituted diphenylamines are expected to have low mobility in soil. Volatilization of most members of substituted diphenylamines from water and moist soil is considered moderate based on their estimated Henry's Law constant, except for CASRN 10081-67-1 and 68442-68-2 which are expected to volatilize slowly. The rate of hydrolysis is considered negligible. The rate of atmospheric photooxidation is considered rapid. Persistence of substituted diphenylamines is expected to range from low to high (P1 to P3). The bioaccumulation potential for the category members also ranges from low (B1) to high (B3).

Table 3. Environmental Fate Characteristics of Substituted Diphenylamines Category						
CASRN	10081-67-1	68411-46-1	68442-68-2	68608-77-5	68921-45-9	184378-08-3
Persistence	P2 (moderate)	P2-3 (moderate-high)	P2 (moderate)	P2-3 (moderate-high)	P2-3 (moderate-high)	P2-3 (moderate-high)
Bioaccumulation	B1 (low)	B1-B3 (low-high)	B2-B3 (moderate-high)	B1 (low)	B2-B3 (moderate-high)	B1-B3 (low-high)

3. Human Health Effects

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

Benzenamine, 4-octyl-N-(4-octylphenyl) (CASRN 101-67-7)

Male and female Sprague-Dawley rats (5/dose) were administered benzenamine, 4-octyl-N-(4-octylphenyl) as a 20.0% suspension in corn oil at 6310 or 7940 mg/kg-bw. No animals died during the 14 days observation period.

LD₅₀ > 7940 mg/kg-bw

Benzenamine, N-phenyl-, styrenated (CASRN 68442-68-2)

(1) Rats (5/dose, strain not specified) were administered benzenamine, N-phenyl-, styrenated as a 25% solution in corn oil via gavage at doses of 2500, 5000, 10,000, 20,000 and 40,000 mg/kg-bw and were observed for 14 days. At each of the two highest doses, two animals died.

LD₅₀ > 20,000 mg/kg-bw

(2) Rats (5/sex/dose, strain not specified) were administered benzenamine, N-phenyl-, styrenated dispersed in corn oil via gavage at 500 mg/kg-bw. No animals died during the 14 days observation period.

LD₅₀ > 500 mg/kg-bw

Benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives (CASRN 68608-77-5)

Rats (2/dose, strain not specified) were administered benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives via gavage at 10,250, 15,380, 23,070 and 34,600 mg/kg-bw and were observed for 14 days. No deaths were reported at any dose.

LD₅₀ > 34,600 mg/kg-bw

Benzenamine, N-phenyl- reaction product with 2,4,4-trimethylpentene and isobutylene (CASRN 184378-08-3)

A group of three female Sprague-Dawley rats were administered a solution of benzenamine, N-phenyl- reaction product with 2,4,4-trimethylpentene and isobutylene in arachis oil via gavage as a single dose of 2000 mg/kg-bw and observed for 14 days. No deaths were observed.

LD₅₀ > 2000 mg/kg-bw

Acute Dermal Toxicity

Benzenamine, 4-octyl-N-(4-octylphenyl) (CASRN 101-67-7)

New Zealand white rabbits (2 males and 1 female) were administered benzenamine, 4-octyl-N-(4-octylphenyl) dermally as a single application of 40.0% suspension in corn oil at 5010 or 7940 mg/kg-bw to the shaved skin under occlusive conditions for 24 hours. All animals survived until sacrifice on day 14.

LD₅₀ > 7940 mg/kg-bw

Benzenamine, N-phenyl-, styrenated (CASRN 68442-68-2)

Rabbits (5/dose, strain not specified) were administered benzenamine, N-phenyl-, styrenated dermally at 10,000 mg/kg-bw. No mortality was reported.

LD₅₀ > 10,000 mg/kg-bw

Benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives (CASRN 68608-77-5)

A group of four New Zealand rabbits (sex not specified) were administered benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives at 3000 mg/kg-bw dermally to a shaved area on the backs under occlusive conditions for 4 hours and observed for 14 days. No mortality was observed.

LD₅₀ > 3000 mg/kg-bw

Repeated-Dose Toxicity

Benzenamine, N-phenyl- reaction products with 2,4,4-trimethylpentene and isobutylene (CASRN 184378-08-3)

In a combined repeated-dose/reproductive/developmental toxicity screening test, Sprague-Dawley (10/sex/dose) were administered benzenamine, N-phenyl-, reaction products with 2,4,4-trimethylpentene and isobutylene via gavage at 0, 5, 25 and 125 mg/kg-bw/day for 43 (males) and 54 (females) days. Pairing of animal within each dose group was undertaken on a one male to one female basis on Day 15 of the study. Males were terminated on Day 43 and all females were terminated on Day 5 post partum (with exposures before and after mating, during gestation and lactation for 4 days). No deaths or treatment-related behavioral changes, functional performance or sensory reactivity were noted at any dose. At 125 mg/kg-bw/day, there was decreased food intake and body weight gain in females during lactation. Hematological evaluation indicated increased levels of activated partial thromboplastin time at 125 mg/kg-bw/day in both sexes. There was a decreased platelet count in both sexes prior to mating. At 125 mg/kg-bw/day, males had elevated absolute and relative liver weights and females had reduced spleen weights. Females at 25 and 125mg/kg-bw/day and males at 125 mg/kg-bw/day had decreased total plasma protein, albumin and the albumin/ globulin ratio and elevated aspartate aminotransferase and alkaline phosphatase activities. Consistent with these biochemical and enzymic effects (indicative of liver toxicity), histopathological evaluation revealed centrilobular hepatocytes enlargement in females at ≥ 25 mg/kg-bw/day and in males at 125 mg/kg-bw/day.

LOAEL (females) = 25 mg/kg-bw/day (based on liver toxicity)

NOAEL (females) = 5 mg/kg-bw/day

LOAEL (males) = 125 mg/kg-bw/day (based on changes in hematological parameters and liver toxicity)

NOAEL (males) = 25 mg/kg-bw/day

Benzenamine, N-phenyl-, reaction products with styrene and 2,4,4-trimethylpentene (CASRN 68921-45-9)

Carworth rats (25/sex/dose) were administered benzenamine, N-phenyl-, reaction products with styrene and 2,4,4-trimethylpentene in the diet at 2500, 5000 and 10,000 ppm (~ 125, 250 and 500 mg/kg-bw/day, respectively) for 64 weeks. Growth retardation (decrease in body weight) was

observed in all treated females. Hepatomegaly was observed in both sexes at all doses. Diffuse hepatic degeneration was observed in all test animals. The degenerative changes in the liver were described as diffuse cloudy swellings and fatty metamorphosis of the cytoplasm of the hepatocytes.

LOAEL ~ 125 mg/kg-bw/day (based on growth retardation/decrease in body weight in females and liver toxicity in both sexes)

NOAEL = Not established

Benzenamine, N-phenyl-, styrenated (CASRN 68442-68-2)

In a combined repeated-dose/reproductive/developmental toxicity screening test, Sprague-Dawley rats (10/sex/dose) were administered benzenamine, N-phenyl-, styrenated suspension in corn oil, via gavage at 0, 50, 250 and 600 mg/kg-bw/day for 43 (males) and 54 (females) days. Pairing of animal within each dose group was undertaken on a one male to one female basis on Day 15 of the study. Males were terminated on Day 43 and all females were terminated on Day 5 post partum (with exposures before and after mating, during gestation and lactation for 4 days). No deaths or treatment-related changes in body weight, growth, food and water intake or behavioral assessments were seen in any treatment groups. However, absolute and relative liver and adrenal weights were increased in both sexes at the 600 mg/kg-bw/day. Reduced cholesterol levels were reported in males at 250 and 600 mg/kg-bw/day, and an increased activity for alkaline phosphatase was noted in males at 600 mg/kg-bw/day; both of these effects are indicative of liver toxicity. Histopathological examination of the liver revealed centrilobular hepatocyte enlargement in all treated females and in males treated with 250 and 600 mg/kg-bw/day. In males, follicular cell hypertrophy in the thyroid glands was also observed at 600 mg/kg-bw/day.

LOAEL = 600 mg/kg-bw/day (based on increased liver and adrenal weights and toxicity in liver and thyroid glands)

NOAEL = 250 mg/kg-bw/day

Reproductive Toxicity

Benzenamine, N-phenyl-, styrenated (CASRN 68442-68-2)

In the combined repeated-dose/reproductive/developmental toxicity screening study described previously, no adverse effects on mating performance, fertility or gestation were observed. Females treated with 600 mg/kg-bw/day had a higher percentage of pre-implantation losses compared to controls, resulting in less offspring/litter when compared to controls and lower total litter weights.

LOAEL (reproductive toxicity) = 600 mg/kg-bw/day (based on higher pre-implantation losses)

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

Benzenamine, N-phenyl- reaction product with 2,4,4-trimethylpentene and isobutylene (CASRN 184378-08-3)

In the combined repeated-dose/reproductive/developmental toxicity screening study described previously, shorter gestation length, lower viability indices and lower total litter weights were seen at 125 mg/kg-be/day.

LOAEL (reproductive toxicity) = 125 mg/kg-bw/day (based on shorter gestation lengths and lower viability indices)

NOAEL (reproductive toxicity) = 25 mg/kg-bw/day

Developmental Toxicity

Benzenamine, N-phenyl-, styrenated (CASRN 68442-68-2)

In the combined repeated-dose/reproductive/developmental toxicity screening study described previously, no clinical signs of toxicity were observed in the offspring. The mean offspring weights of treated animals were comparable to controls. Offspring from the 600 mg/kg-bw/day treated animals showed less successful completion of surface righting assessments. No treatment-related macroscopic abnormalities were observed at necropsy.

LOAEL (maternal toxicity) = 600 mg/kg-bw/day (based on increased liver and adrenal weights and toxicity in liver and thyroid glands)

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

LOAEL (developmental toxicity) = 600 mg/kg-bw/day (based on diminished surface righting assessments)

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

Benzenamine, N-phenyl- reaction product with 2,4,4-trimethylpentene and isobutylene (CASRN 184378-08-3)

In the combined repeated-dose/reproductive/developmental toxicity screening study described previously, the number of interim deaths of offsprings at 125 mg/kg-bw/day was higher than that observed for controls. At the same dose, the mean offspring body weights were also lower. No other treatment-related effects were observed on offspring development.

LOAEL (maternal toxicity) = 25 mg/kg-bw/day (based on liver toxicity)

NOAEL (maternal toxicity) = 5 mg/kg-bw/day

LOAEL (developmental toxicity) = 125 mg/kg-bw/day (based on decrease in offspring viability indices and offspring body weight)

NOAEL (developmental toxicity) = 25 mg/kg-bw/day

Genetic Toxicity – Gene Mutation

In vitro

Benzenamine, 4-octyl-N-(4-octylphenyl) (CASRN 101-67-7)

(1) *Salmonella typhimurium* strains were exposed to benzenamine, 4-octyl-N-(4-octylphenyl) at concentrations up to 500 µg/plate with and without metabolic activation. Positive and negative controls were used; however, their responses were not provided.

Benzenamine, 4-octyl-N-(4-octylphenyl) was not mutagenic in this assay.

(2) *Saccharomyces cerevisiae*, D4, were exposed to benzenamine, 4-octyl-N-(4-octylphenyl) at concentrations up to 500 µg/plate with and without metabolic activation. Positive and negative controls were used; however, their responses were not provided..

Benzenamine, 4-octyl-N-(4-octylphenyl) was not mutagenic in this assay.

Benzenamine, N-phenyl-, styrenated (CASRN 68442-68-2)

S. typhimurium and *Escherichia coli* strains were exposed to benzenamine, N-phenyl-, styrenated at concentrations up to 5000 µg/plate with and without metabolic activation. The vehicle and positive controls responded appropriately.

Benzenamine, N-phenyl-, styrenated was not mutagenic in this assay.

Benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives (CASRN 68608-77-5)

S. typhimurium and *E. coli* strains were exposed to benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives in two separate assays at concentrations up to 5000 µg/plate with and without metabolic activation. The positive controls responded appropriately.

Benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives was not mutagenic in these assays.

Benzenamine, N-phenyl-, reaction products with styrene and 2,4,4-trimethylpentene (CASRN 68921-45-9)

S. typhimurium and *E. coli* were exposed to benzenamine, N-phenyl-, reaction products with styrene and 2,4,4-trimethylpentene at concentrations up to 5000 µg/plate with and without metabolic activation. The vehicle and positive controls responded appropriately.

Benzenamine, N-phenyl-, reaction products with styrene and 2,4,4-trimethylpentene was not mutagenic in this assay.

Benzenamine, N-phenyl- reaction product with 2,4,4-trimethylpentene and isobutylene (CASRN 184378-08-3)

S. typhimurium strains were exposed to benzenamine, N-phenyl-, reaction products with 2,4,4-trimethylpentene and isobutylene at concentrations up to 5000 µg/plate with and without metabolic activation. The vehicle and positive controls responded appropriately.

Benzenamine, N-phenyl-, reaction products with 2,4,4-trimethylpentene and isobutylene was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vitro

Benzenamine, 4-octyl-N-(4-octylphenyl) (CASRN 101-67-7)

Chinese hamster ovary (CHO) and lung (CHL) cells were exposed to benzenamine, 4-octyl-N-(4-octylphenyl) at concentrations up to 4.45 mg/mL and 0.5 mg/mL, respectively, with and without metabolic activation. The controls responded appropriately.

Benzenamine, 4-octyl-N-(4-octylphenyl) did not induce chromosomal aberrations in this assay.

In vivo

Benzenamine, N-phenyl-, styrenated (CASRN 68442-68-2)

CD-1 mice (5 males/dose) were administered single doses of benzenamine, N-phenyl-, styrenated in corn oil, via gavage at 0, 500, 1000 and 2000 mg/kg-bw/day. Bone marrow cells were harvested 24 and 48 hours after dosing. Slides were prepared from the bone marrow extracts and 2000 micronucleated polychromatic erythrocytes were evaluated for the presence of micronuclei. The ratio of polychromatic erythrocytes (PCE) to nonchromatic erythrocytes

(NCE) cells was determined. Low PCE:NCE ratios indicated that benzenamine, N-phenyl-, styrenated was cytotoxic to bone marrow.

Benzenamine, N-phenyl-, styrenated did not induce chromosomal aberrations in this assay.

Genetic Toxicity – Other

Benzenamine, 4-octyl-N-(4-octylphenyl) (CASRN 101-67-7)

In a sister chromatid exchange assay, CHO cells were exposed to benzenamine, 4-octyl-N-(4-octylphenyl) at concentrations up to 5 mg/L with and without metabolic activation. The controls responded appropriately.

Benzenamine, 4-octyl-N-(4-octylphenyl) did not induce sister chromatid exchange in this assay.

Benzenamine, N-phenyl-, styrenated (CASRN . 68442-68-2)

In an *in vitro* DNA damage and repair assay, *E. coli* strains W3110 and p3478 were exposed to benzenamine, N-phenyl-, styrenated up to 5000 µg/L with and without metabolic activation. Negative and positive controls were used.

Benzenamine, N-phenyl-, styrenated did not damage cellular DNA in this assay.

Additional Information

Eye Irritation

Benzenamine, 4-octyl-N-(4-octylphenyl) (CASRN 101-67-7)

New Zealand White rabbits (6/dose) were instilled in one eye with 100 mg of benzenamine, 4-octyl-N-(4-octylphenyl) as a finely ground powder moistened with water. The other eye was not treated and served as the control. Slight discomfort was noted immediately following instillation. At 10 minutes, slight erythema and slight discharge were noted. At 24 hours, there was slight erythema and moderate discharge in all test animals. At 48 hours, two of the six had slight erythema and slight discharge. All signs of irritation had subsided by the third day post-exposure.

Benzenamine, 4-octyl-N-(4-octylphenyl) was slightly irritating to rabbit eyes in this study.

Benzenamine, N-phenyl-, styrenated (CASRN 68442-68-2)

Albino rabbits (6, sex not stated) were instilled into in one eye with benzenamine, N-phenyl-, styrenated; the other eye was not treated and served as the control. Three rabbits had the test substance rinsed out of the eye with water and three rabbits did not. Mild eye irritation was noted in the eyes that were not rinsed.

Benzenamine, N-phenyl-, styrenated was slightly irritating to rabbit eyes in this study.

Benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives (CASRN 68608-77-5)

Benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives was slightly irritating to the eye when tested in New Zealand white rabbits. Additional information was not provided.

Benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives was slightly irritating to rabbit eyes in this study.

Skin Irritation

Benzenamine, 4-octyl-N-(4-octylphenyl) (CASRN 101-67-7)

New Zealand White rabbits (6/dose) were applied 0.5 g benzenamine, 4-octyl-N-(4-octylphenyl) as a finely ground powder moistened with water to the shaved dorsal area under occlusive conditions for 24 hours. Dermal irritation was scored by the Draize method and results were recorded 24, 48, 72 and 168 hours after application. No irritation was noted.

Benzenamine, 4-octyl-N-(4-octylphenyl) was not irritating to rabbit skin in this study.

Benzenamine, N-phenyl-, styrenated (CASRN 68442-68-2)

Benzenamine, N-phenyl-, styrenated was considered a mild irritant to rabbit skin according to current classifications (it was originally classified as non-irritating). Study details were not provided.

Benzenamine, N-phenyl-, styrenated was slightly irritating to rabbit skin in this study.

Skin Sensitization

Benzenamine, N-phenyl- reaction product with 2,4,4-trimethylpentene and isobutylene (CASRN 184378-08-3)

In a guinea pig maximization test, Dunkin Hartley guinea pigs (10/dose) were administered benzenamine, N-phenyl- reaction product with 2,4,4-trimethylpentene and isobutylene as a 25% solution in either arachis oil BP or 25% in arachis oil BP in a 1:1 preparation of Freund's Complete Adjuvant in water via intradermal injection during the induction phase. The application sites were evaluated at 24 and 48 hours. After 7 days, induction was initiated by applying undiluted test substance was applied to the same area as the previous injections on the clipped shoulder region and covered by an occlusive patch. On day 21, topical challenge proceeded with application of an undiluted test substance and a 75% solution (in arachis oil BP) to a clipped area and covered with an occlusive patch for 24 hours. No sensitization was observed.

Benzenamine, N-phenyl-, reaction products with styrene and 2,4,4-trimethylpentene was not sensitizing in this test.

Benzenamine, N-phenyl-, reaction products with styrene and 2,4,4-trimethylpentene (CASRN 68921-45-9)

In a patch test, volunteers (25/sex) were treated with benzenamine, N-phenyl- reaction product with 2,4,4-trimethylpentene on the identical spots on the back for 24 hours every other day for 15 applications. Two weeks after the induction period, the sites were challenged with test material for 24 hours. A minimal transitory reaction was noted in three males and four females. No depigmentation was noted.

Benzenamine, N-phenyl-, reaction products with styrene and 2,4,4-trimethylpentene was not considered to be a primary irritant, fatiguing agent or sensitizer in this test.

Conclusion: The acute oral toxicity of category members CASRN 68442-68-2, 184378-08-3, 101-67-7 and 68608-77-5 in rats is low, and the acute dermal toxicity of three of them (CASRN 68442-68-2, 101-67-7 and 68608-77-5) in rabbits is also low. A combined repeated-dose/

reproductive/ developmental toxicity study by the oral route in rats with category member CASRN 184378-08-3 showed hematological and hepatic toxicity at 125 mg/kg/day in males and hepatic toxicity at 25 mg/kg/day in females; the NOAEL for systemic toxicity for male rats was 25 mg/kg/day; the NOAEL for systemic and maternal toxicity for female rats was 5 mg/kg/day. In the same study, there was reproductive toxicity at 125 mg/kg/day as demonstrated by shorter gestations lengths and lower viability indices; the NOAEL for reproductive toxicity was 25 mg/kg/day. There was evidence of developmental toxicity in this study as demonstrated by decreases in offspring viability and body weights at 125 mg/kg/day; the NOAEL for developmental toxicity was 25 mg/kg/day. A repeated-dose toxicity study by the oral route in rats with CASRN 68921-45-9 showed decreased body weights and liver toxicity at 125 mg/kg/day, the lowest dose, the NOAEL for systemic toxicity is not established. An oral combined repeated-dose/reproductive/ developmental toxicity screening study in rats with category member 68442-68-2 showed increased liver and adrenal weights and toxicity of the liver and thyroid glands-at 600 mg/kg/day; the NOAEL for systemic and maternal toxicity was 250 mg/kg-bw/day. In the same study, there was reproductive toxicity at 600 mg/kg/day as demonstrated by higher pre-implantation losses; the NOAEL for reproductive toxicity was 250 mg/kg/day. There was evidence of developmental toxicity as demonstrated by diminished surface righting at 600 mg/kg-bw/day; the NOAEL for developmental toxicity was 250 mg/kg/day. Category members did not induce gene mutations or chromosomal aberrations when tested *in vitro* or *in vivo*. Category member CASRN 68442-68-2 is slightly irritating to both the eyes and skin; category members CASRN 101-67-7 and 68608-77-5 are slightly irritating to the eyes. Skin irritation was not observed with category members CASRN 68921-45-9 and 101-67-7. Category members CASRN 68921-45-9 and 184378-08-3 are not dermal sensitizers.

Table 4. Summary of Human Health Data								
Endpoints	Benzenamine, N-phenyl-, styrenated (68442-68-2)	Benzenamine, N-phenyl-, reaction products with styrene and 2,4,4-trimethyl-pentene (68921-45-9)	Benzenamine, N-phenyl-, reaction products with 2,4,4-trimethyl-pentene (68411-46-1)	Benzenamine, N-phenyl-, reaction product with 2,4,4-trimethyl-pentene and isobutylene (184378-08-3)	Benzenamine, 4-(1-methyl-1-phenylethyl)-N-4[4-(1-methyl-1-phenylethyl)phenyl]- (10081-67-1)	Benzenamine, 4-octyl-N-(4-octylphenyl) (101-67-7)	Benzenamine, ar-nonyl-N-nonylphenyl (36878-20-3)	Benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives (68608-77-5)
Acute Oral Toxicity LD ₅₀ (mg/kg-bw)	> 20,000	No Data > 2000 (RA)	No Data > 2000 (RA)	> 2000	No Data > 2000 (RA)	> 7940	No Data > 2000 (RA)	> 34,600
Acute Dermal Toxicity LD ₅₀ (mg/kg-bw)	> 10,000	No Data > 3000 (RA)	No Data > 3000 (RA)	No Data > 3000 (RA)	No Data > 3000 (RA)	> 7940	No Data > 3000 (RA)	> 3000
Repeated-Dose Toxicity NOAEL/LOAEL (mg/kg-bw/day)	NOAEL = 250 LOAEL = 600	NOAEL = Not established LOAEL ~ 125	No Data NOAEL(f) = 5 LOAEL(f) = 25 NOAEL(m) = 25 LOAEL(m) = 125 (RA)	NOAEL(f) = 5 LOAEL(f) = 25 NOAEL(m) = 25 LOAEL(m) = 125	No Data NOAEL(f) = 5 LOAEL(f) = 25 NOAEL(m) = 25 LOAEL(m) = 125 (RA)	No Data NOAEL(f) = 5 LOAEL(f) = 25 NOAEL(m) = 25 LOAEL(m) = 125 (RA)	No Data NOAEL(f) = 5 LOAEL(f) = 25 NOAEL(m) = 25 LOAEL(m) = 125 (RA)	No Data NOAEL(f) = 5 LOAEL(f) = 25 NOAEL(m) = 25 LOAEL(m) = 125 (RA)
Reproductive Toxicity NOAEL/LOAEL (mg/kg-bw/day)	NOAEL = 250 LOAEL = 600	No Data NOAEL = 25 LOAEL = 125 (RA)	No Data NOAEL = 25 LOAEL = 125 (RA)	NOAEL = 25 LOAEL = 125	No Data NOAEL = 25 LOAEL = 125 (RA)	No Data NOAEL = 25 LOAEL = 125 (RA)	No Data NOAEL = 25 LOAEL = 125 (RA)	No Data NOAEL = 25 LOAEL = 125 (RA)
Developmental Toxicity NOAEL/LOAEL (mg/kg-bw/day) Maternal Toxicity	NOAEL = 250 LOAEL = 600	No Data NOAEL = 5 LOAEL = 25	No Data NOAEL = 5 LOAEL = 25	NOAEL = 5 LOAEL = 25	No Data NOAEL = 5 LOAEL = 25	No Data NOAEL = 5 LOAEL = 25	No Data NOAEL = 5 LOAEL = 25	No Data NOAEL = 5 LOAEL = 25
Developmental Toxicity	NOAEL = 250 LOAEL = 600	NOAEL = 25 LOAEL = 125 (RA)	NOAEL = 25 LOAEL = 125 (RA)	NOAEL = 25 LOAEL = 125	NOAEL = 25 LOAEL = 125 (RA)	NOAEL = 25 LOAEL = 125 (RA)	NOAEL = 25 LOAEL = 125 (RA)	NOAEL = 25 LOAEL = 125 (RA)
Genetic Toxicity –			No Data		No Data		No Data	

Table 4. Summary of Human Health Data								
Endpoints	Benzenamine, N-phenyl-, styrenated (68442-68-2)	Benzenamine, N-phenyl-, reaction products with styrene and 2,4,4-trimethylpentene (68921-45-9)	Benzenamine, N-phenyl-, reaction products with 2,4,4-trimethylpentene (68411-46-1)	Benzenamine, N-phenyl-, reaction product with 2,4,4-trimethylpentene and isobutylene (184378-08-3)	Benzenamine, 4-(1-methyl-1-phenylethyl)-N-4[4-(1-methyl-1-phenylethyl)phenyl]- (10081-67-1)	Benzenamine, 4-octyl-N-(4-octylphenyl) (101-67-7)	Benzenamine, ar-nonyl-N-nonylphenyl (36878-20-3)	Benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives (68608-77-5)
Gene Mutation <i>In vitro</i>	Negative	Negative	Negative (RA)	Negative	Negative (RA)	Negative	Negative (RA)	Negative
Genetic Toxicity – Chromosomal Aberrations <i>In vitro</i>	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	Negative	No Data Negative (RA)	No Data Negative (RA)
Genetic Toxicity – Other								
DNA damage and repair (<i>in vitro</i>)	Negative	—*	—*	—*	—*	—*	—*	—*
Mouse micronucleus (<i>in vivo</i>)	Negative	—*	—*	—*	—*	—*	—*	—*
Sister chromatid exchange	—*	—*	—*	—*	—*	Negative	—*	—*
Additional Information								
Skin Irritation	Slightly irritating	Not irritating	—*	—*	—*	Not irritating	—*	—*
Eye Irritation	Slightly irritating	—*	—*	—*	—*	Slightly irritating	—*	Slightly irritating
Sensitization	—*	Negative	—*	Negative	—*	—*	—*	—*

Measured data in bold text; (RA) = Read Across; (f) = females; (m) = males; – indicates endpoint was not addressed for this chemical; * indicates endpoint is not included in the base data set under the HPV Challenge Program.

4 Hazards to the Environment

A summary of aquatic toxicity data submitted for SIDS endpoints 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.

Acute Toxicity to Fish

Benzenamine, 4-octyl-N-(4-octylphenyl) (CASRN 101-67-7)

(1) Bluegill sunfish (*Lepomis macrochirus*) were exposed to benzenamine, 4-octyl-N-(4-octylphenyl) at a nominal concentration range of 100 – 1000 mg/L, in a closed system under static conditions for 96 hours. Acetone was used as the solvent and solvent control. A 96-h LC₅₀ of > 1000 mg/L was reported. The results of this test are difficult to interpret because the substance was tested above its water solubility limit and in the presence of solvent. Therefore, EPA considers the no effect concentration to be the water solubility limit (saturation), which for benzenamine, 4-octyl-N-(4-octylphenyl) would be approximately 4.215×10^{-7} mg/L.

No effects at saturation

(2) Rainbow trout (*Salmo gairdneri*) were exposed to benzenamine, 4-octyl-N-(4-octylphenyl) at a nominal concentration range of 100 – 1000 mg/L, in a closed system under static conditions for 96 hours. Acetone was used as the solvent and solvent control. A 96-h LC₅₀ of > 1000 mg/L was reported. The results of this test are difficult to interpret because the substance was tested above its water solubility limit and in the presence of solvent. Therefore, EPA considers the no effect concentration to be the water solubility limit (saturation), which for benzenamine, 4-octyl-N-(4-octylphenyl) would be approximately 4.215×10^{-7} mg/L.

No effects at saturation

Benzenamine, ar-nonyl-N-nonylphenyl (CASRN 36878-20-3)

Fathead minnows (*Pimephales promelas*) were exposed to benzenamine, ar-nonyl-N-nonylphenyl at a nominal concentration range of 1000 – 10,000 mg/L, under semi-static conditions for 96 hours. Benzenamine, ar-nonyl-N-nonylphenyl was renewed after 48 hours. No mortality was observed at the highest concentration tested. The results of this test are difficult to interpret because the substance was tested above its water solubility limit. Therefore, EPA considers the no effect concentration as the water solubility limit (saturation).

No effects at saturation

Benzenamine, N-phenyl-, styrenated (CASRN 68442-68-2)

Zebrafish (*Brachydanio rerio*) were exposed to benzenamine, N-phenyl-, styrenated at nominal concentrations under static conditions for 96 hours. The benzenamine, N-phenyl-, styrenated was dispersed in water by means of an Ultra-Turrax. Mortality increased with increasing concentration of benzenamine, N-phenyl-, styrenated added to the test solution and the sponsor reported 96-h LC₅₀ of 920 mg/L. The results of this test are difficult to interpret because the substance was tested above its water solubility limit, but are likely due to physical effects because tested concentrations vastly exceeded the water solubility limit (saturation), which for benzenamine, N-phenyl-, styrenated is 0.41 mg/L.

No effects at saturation

Acute Toxicity to Aquatic Invertebrates

Benzenamine, 4-octyl-N-(4-octylphenyl) (CASRN 101-67-7)

Daphnia magna were exposed to benzenamine, 4-octyl-N-(4-octylphenyl) at a nominal concentration range of 1.8 –32 mg/L, in a closed system under static conditions for 48 hours. DMF was used as the solvent and solvent control. Mortality increased with increasing concentration of benzenamine, 4-octyl-N-(4-octylphenyl) added to the test solution and the sponsor reported 48-h EC₅₀ of 7.7 mg/L. The results of this test are difficult to interpret because the substance was tested above its water solubility limit and in the presence of solvent, but are likely due to physical effects because tested concentrations vastly exceeded the water solubility limit (saturation), which for benzenamine, 4-octyl-N-(4-octylphenyl) is approximately 4.215×10^{-7} mg/L.

No effects at saturation

Benzenamine, ar-nonyl-N-nonylphenyl (CASRN 36878-20-3)

Crustacea (*Mysidopsis bahia*) were exposed to benzenamine, ar-nonyl-N-nonylphenyl as water accommodated fractions (WAFs) under semi-static conditions for 96 hours. The loading rates were 0, 150, 250, 400, 600 or 1000 mg/L and no analytical measurements were made on the WAFs. EPA does not consider the loading rate as the no effect concentration when the concentration exceeds the water solubility of the test substance. The results of this test are difficult to interpret because the substance was tested above its water solubility limit, but are likely due to physical effects because the tested concentrations vastly exceeded the water solubility limit (saturation).

No effects at saturation

Toxicity to Aquatic Plants

Benzenamine, ar-nonyl-N-nonylphenyl (CASRN 36878-20-3)

Algae (*Pseudokirchneriella subcapitata*) were exposed to benzenamine, ar-nonyl-N-nonylphenyl as water accommodated fractions (WAFs) under static conditions for 96 hours. The loading rates were 0, 0.3, 3.3, 33, 330 or 3300 mg/L and no analytical measurements were made on the WAFs. Effects observed at 330 mg/L were determined to be algistatic based on the rapid re-growth of an aliquot of cells taken from 500 mg/L cultured in fresh control media. EPA does not consider the loading rate as the no effect concentration when the concentration exceeds the water solubility of the test substance. The results of this test are difficult to interpret because the substance was tested above its water solubility limit, but are likely due to physical effects because the tested concentrations vastly exceeded the water solubility limit (saturation),

No effects at saturation

Conclusion: The measured acute toxicity values of substituted diphenylamines to fish aquatic invertebrate and aquatic plants have no effects at the saturation limit (4.2×10^{-7} mg/L).

Table 5. Summary of Environmental Effects – Aquatic Toxicity Data								
Endpoints	Benzenamine, N-phenyl-, styrenated (68442-68-2)	Benzenamine, N-phenyl-, reaction products with styrene and 2,4,4-trimethylpentene (68921-45-9)	Benzenamine, N-phenyl-, reaction products with 2,4,4-trimethylpentene (68411-46-1)	Benzenamine, N-phenyl-, reaction products with 2,4,4-trimethylpentene and isobutylene (184378-08-3)	Benzenamine, 4-(1-methyl-1-phenylethyl)-N-4[4-(1-methyl-1-phenylethyl) phenyl]- (10081-67-1)	Benzenamine, 4-octyl-N-(4-octylphenyl) (101-67-7)	Benzenamine, ar-nonyl-N-nonylphenyl (36878-20-3)	Benzenamine, 2-ethyl-N-(2-ethylphenyl)-, (tripropenyl) derivatives (68608-77-5)
Fish 96-h LC₅₀ (mg/L)	NES	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	NES	NES	No Data NES (RA)
Aquatic Invertebrates 48-h EC₅₀ (mg/L)	NES	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	NES	No Data NES (RA)	No Data NES (RA)
Aquatic Plants 72-h EC₅₀ (mg/L)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	No Data NES (RA)	NES	No Data NES (RA)

RA = read across, NES = No effect at saturation