

## SCREENING-LEVEL HAZARD CHARACTERIZATION

### Cyclohexane, oxidized, aq. ext. (CASRN 68915-38-8)

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

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

The evaluation is performed according to established EPA guidance<sup>2,3</sup> and is based primarily on hazard data provided by sponsors; however, in preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor’s responses to comments and revisions made to the submission. In order to determine whether any new hazard information was developed since the time of the HPV submission, a search of the following databases was made from one year prior to the date of the HPV Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, 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.

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

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

<sup>3</sup> U.S. EPA. Risk Assessment Guidelines; <http://cfpub.epa.gov/ncea/raf/rafguid.cfm>.

These hazard characterizations are technical documents intended to inform subsequent decisions and actions by OPPT. Accordingly, the documents are not written with the goal of informing the general public. However, they do provide a vehicle for public access to a concise assessment of the raw technical data on HPV chemicals and information previously not readily available to the public.

<b>Chemical Abstract Service Registry Number (CASRN)</b>	<b>68915-38-8</b>
<b>Chemical Abstracts Index Name</b>	<b>Cyclohexane, oxidized, aq. ext.</b>
<b>Structural Formula</b>	(see Section 1)

### Summary

Cyclohexane, oxidized, aqueous extract (CASRN 68915-38-8) is expected to have high mobility in soil. A mixture of the dicarboxylic acid solution: water (42.9%), free carboxylic acids (27.8%) and alcohols (13.3%) was shown to be readily biodegradable. Adipic acid (CASRN 124-04-9), one of the primary components of CASRN 68915-38-8, is also readily biodegradable. The rate of volatilization of CASRN 68915-38-8 from water and moist soil is considered low since carboxylic acids exist as anions under environmental conditions. The rate of hydrolysis is considered negligible. CASRN 68915-38-8 is expected to have low persistence (P1) and low bioaccumulation potential (B1).

The acute oral toxicity of CASRN 68915-38-8 is low; the oral LD<sub>50</sub> is > 5000 mg/kg-day in rats. Genotoxicity studies represent the only other health hazard data that is available for the sponsored chemical. CASRN 124-04-9 is one of the most abundant carboxylic acid components in CASRN 68915-38-8. Although EPA agrees that use of CASRN 124-04-9 as a supporting chemical for CASRN 68915-38-9 may be reasonable, there are other pending issues. A two-year feeding study conducted with CASRN 124-04-9 revealed significant decreases in body weight gain in male rats treated at doses of 2250 mg/kg-bw/day or higher; however, there was no overall effect on body weight. The NOAEL for systemic toxicity is 750 mg/kg-bw/day (based on dose-related decreases in body weight gain). Prenatal developmental toxicity studies with CASRN 124-04-9 showed no treatment-related maternal or developmental effects following oral gavage at the highest dose tested in rats (288 mg/kg-day) or rabbits (250 mg/kg-day). Reproductive studies were not performed; however, an evaluation of reproductive organs in the two-year feeding study described above did not show any evidence of toxicity in reproductive tissues (testes, ovaries and uteri). Both skin and eye irritation were observed following topical application of CASRN 124-04-9 in rabbits. CASRN 124-04-9 did not induce gene mutations *in vitro* or chromosomal aberrations *in vivo*. CASRN 124-04-9 may be a reasonable choice for supporting chemical given the likely metabolism of 6-hydroxycaproic acid (CASRN 1191-25-9) to CASRN 124-04-9; however, EPA believes that *in vitro* studies documenting the rate of metabolic conversion are warranted, given uncertainties regarding the reaction kinetics associated with aldehyde formation.

The measured 96-hour LC<sub>50</sub> of CASRN 68915-38-8 to fish is 316 mg/L. The measured 48-hour EC<sub>50</sub> of CASRN 68915-38-8 to aquatic invertebrates is >100 mg/L. The measured 72-hour EC<sub>50</sub> of CASRN 68915-38-8 to aquatic plants is >100 mg/L for growth and 92 mg/L for biomass.

Since inadequate information was provided for the purported metabolism of CASRN 1191-25-9 to CASRN 124-04-9, the repeated-dose/reproductive/developmental toxicity endpoints remain as data gaps under the HPV Challenge Program.

## Introduction

The sponsor, BASF Corporation, submitted a Test Plan and Robust Summaries to EPA for cyclohexane, oxidized, aqueous extract (CASRN 68915-38-8) on December 30, 2003. EPA posted the submission on the ChemRTK HPV Challenge website on February 27, 2004 (<http://www.epa.gov/chemrtk/pubs/summaries/cyclhxox/c15012tc.htm>). EPA comments on the original submission were posted to the website on March, 15, 2005. Public comments were also received and posted to the website. The sponsor submitted a response to EPA comments on May 9, 2005, which was posted to the ChemRTK website on June 7, 2005. The sponsor submitted a revised Test Plan and Robust Summaries to EPA on September 16, 2009.

### **“Closed-System Intermediate” (CSI) Status and Analog Justification**

The aqueous extract of oxidized cyclohexane (CASRN 68915-38-8; designated “EP-306” by BASF Corporation) is an aqueous mixture of monocarboxylic acids (C1 – C6), dicarboxylic acids (C4-C6), 6-hydroxycaproic acid, esters of alcoholic and acidic components and trace amounts of oxidized cyclohexane.

Upon review of the original submission, EPA and public comments, as well as the revised test plan and robust summaries, EPA has concluded: 1) EP-306 production described in the revised Test Plan and reported as “site-limited” does not qualify for “closed system intermediate” status<sup>4</sup>; 2) most of the unidentified esters may ultimately be converted to adipic acid; 3) use of adipic acid hazard data (for characterizing repeated-dose/reproductive/developmental toxicity) may be reasonable given the likely metabolism of 6-hydroxycaproic acid to adipic acid. However, because no information on the reaction kinetics associated with metabolic conversion of 6-hydroxycaproic acid to adipic acid were provided, there is a need for quantitative *in vitro* data documenting reaction rates for the alcohol to aldehyde conversion and the subsequent aldehyde to acid conversion in order to demonstrate that the aldehyde intermediate is short lived.

Adipic acid has been reviewed in the OECD program:  
(<http://cs3-hq.oecd.org/scripts/hpv/>).

## 1. **Chemical Identity**

### 1.1 **Identification and Purity**

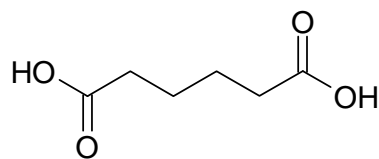
Purification of cyclohexanone is accomplished in part, via a water wash to remove most of the soluble mono- and dicarboxylic acids from the oxidized cyclohexane stream. This water wash is then concentrated to form EP-306, which primarily consists of water, adipic acid and 6-hydroxycaproic acid.

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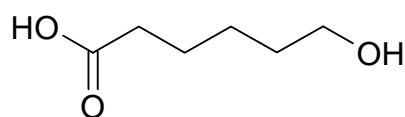
<sup>4</sup> Internal memorandum from F.C. Arnold to S. Oxendine dated October 2, 2009 entitled, *Classification of Cyclohexane Oxidized, Aq. Ext. as a Closed System Intermediate, HPV Case No. SN317*

Typical composition of the EP-306 mixture, as reported in the original submission is shown in Table 1.

Figure 1: Structures of Adipic acid and 6-Hydroxycaproic acid



Adipic acid (CASRN 124-04-9)



6-Hydroxycaproic acid (CASRN 1191-25-9)

**Table 1. Typical Composition of EP-306 (Weight %)**

Formic acid	1 – 3
Acetic acid	0.05 - 0.3
Propionic acid	0.05 – 0.3
Butyric acid	0.2 – 0.6
Valeric acid	0.2 – 0.6
Caproic acid	0.05 - 0.1
Succinic acid	0.3 – 1
Glutaric acid	1 – 2
<b>Adipic acid</b>	<b>12 – 24</b>
<b>6-Hydroxycaproic acid</b>	<b>10 – 14</b>
Cyclohexanol	0.1 – 0.4
Cyclohexanone	0.05 – 0.2
Cyclohexyl Hydroperoxide	0.1 – 0.2
Other*	5 – 10
<b>Water</b>	<b>40 – 60</b>

\*Primarily esters of 6-hydroxycaproic acid and acidic components

Bold font indicates primary components of mixture

## 1.2 Physical-Chemical Properties

The physical-chemical properties are summarized in Table 2. Cyclohexane, oxidized, aqueous extract is a liquid/solid mixture whose components have high water solubility and low to moderate vapor pressure.

<b>Property</b>	<b>Value</b>
Molecular Weight	Variable
Physical State	Liquid/solid mixture
Melting Point	adipic acid: 152 °C
Boiling Point	adipic acid: 337.5 °C
Vapor Pressure	adipic acid: $3.18 \times 10^{-7}$ mm Hg at 25 °C
Water Solubility (mg/L)	adipic acid: 30,800
Dissociation Constant (pK <sub>a</sub> )	4.4 (measured value for adipic acid) <sup>2</sup>
Henry's Law Constant	$2.8 \times 10^{-10}$ to $1.5 \times 10^{-11}$ atm-m <sup>3</sup> /mole (estimated values for adipic and 6-hydroxycaproic acid) <sup>3</sup>
Log K <sub>ow</sub>	adipic acid: 0.08

<sup>1</sup>BASF Corporation. May 9, 2005. Revised Robust Summary and Test Plan for Cyclohexane, Oxidized, Aq. Ext. <http://www.epa.gov/chemrtk/pubs/summaries/cyclhxox/c15012tc.htm>.

<sup>2</sup>SRC. The Physical Properties Database (PHYSPROP). Syracuse, NY: Syracuse Research Corporation. Accessed on October 15, 2008. <http://www.syrres.com/esc/physprop.htm>.

<sup>3</sup>U.S. EPA. 2008. Estimation Programs Interface Suite™ (version 3.20). United States Environmental Protection Agency, Washington, DC, USA. Available online at: <http://www.epa.gov/opptintr/exposure/pubs/episuite.htm>.

## **2. General Information on Exposure**

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

Cyclohexane, oxidized, aqueous extract had an aggregated production volume in the United States of 50 million to 100 million pounds during calendar year 2005.

Non-confidential information in the IUR indicated that the industrial processing and uses for cyclohexane, oxidized, aqueous extract include processing as an intermediate in other basic organic chemical manufacturing.

### **2.2 Environmental Exposure and Fate**

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

The environmental fate properties are provided in Table 3. Cyclohexane, oxidized, aqueous extract is expected to have high mobility in soil. A mixture of dicarboxylic acid solution: water (42.9%), free carboxylic acids (27.8%), and alcohols (13.3%) was shown to be readily biodegradable. Adipic acid, one of the main components of cyclohexane, oxidized, aqueous extract was also found to be readily biodegradable. The rate of volatilization of cyclohexane, oxidized, aqueous extract from water and moist soil is considered low since carboxylic acids exist as anions under environmental conditions. The rate of hydrolysis is considered negligible. Cyclohexane, oxidized, aqueous extract is expected to have low persistence (P1) and low bioaccumulation potential (B1).

Property	Value
Photodegradation Half-life	0.6–20 days (estimated values for components of EP-306)
Hydrolysis Half-life	>1 year at pH 5–9
Biodegradation	70–80% after 28 days (readily biodegradable); 85–90% after 14 days (adipic acid) (readily biodegradable) <sup>2</sup>
Bioconcentration	BCF = 3.162 (estimated values for adipic and 6-hydroxycaproic acid) <sup>3</sup>
Log K <sub>oc</sub>	0 to 1.33 (estimated values for adipic acid and 6-hydroxycaproic acid) <sup>3</sup>
Fugacity (estimated for analogs using Level III Model)	Air = <0.01–0.315% Water = 99.5–99.9% Soil = <0.001–0.03% Sediment = 0.15–0.26%
Persistence <sup>4</sup>	P1 (low)
Bioaccumulation <sup>4</sup>	B1 (low)

<sup>1</sup>BASF Corporation. May 9, 2005. Revised Robust Summary and Test Plan for Cyclohexane, Oxidized, Aq. Ext. <http://www.epa.gov/chemrtk/pubs/summaries/cyclhxox/c15012tc.htm>.

<sup>2</sup>National Institute of Technology and Evaluation. 2002. Biodegradation and Bioaccumulation of the Existing Chemical Substances under the Chemical Substances Control Law. [http://www.safe.nite.go.jp/english/kizon/KIZON\\_start\\_hazkizon.html](http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html).

<sup>3</sup>U.S. EPA. 2008. Estimation Programs Interface Suite™ (version 3.20). United States Environmental Protection Agency, Washington, DC, USA. Available online at: <http://www.epa.gov/opptintr/exposure/pubs/episuite.htm>.

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

### 3. Human Health Hazard

The human health toxicity data are summarized in Table 4.

#### *Acute Oral Toxicity*

Wistar rats (5/sex/dose) were administered cyclohexane, oxidized, aqueous extract via oral gavage at 681, 2150, 3160 or 5000 mg/kg-day and observed for 21 days. Mortalities occurred at doses ≥ 2150 mg/kg-day (3/10 animals at highest dose). Clinical signs of toxicity included apathy, dyspnea, staggered and spastic gait, piloerection and a poor general state.

**LD<sub>50</sub> > 5000 mg/kg-day**

#### *Repeated-Dose Toxicity*

##### *Adipic acid (CASRN 124-04-9; supporting chemical)*

In an oral repeated-dose toxicity study, male and female rats (Carworth Farm strain) were fed a diet containing 0, 0.1, 1, 3 or 5% adipic acid (~ 0, 75, 750, 2250 or 3750 mg/kg-bw/day; 20 males per dose group) or 0 or 1% adipic acid (10 control and 19 females in the 1% treatment group) for two years. Survival rates were similar among treated and control groups. Weight gains were significantly decreased in the 3 and 5% treatment groups (level of significance not specified). Food consumption was normal in all groups except the 5% group, which experienced a consistent reduction in food intake. There were no significant

differences in organ weights of test or control animals at autopsy (kidney, spleen, heart in males and females; brain, thyroid, lungs, liver, adrenals, testes in males only). No treatment-related (gross or microscopic) abnormalities were reported in this study. Information not provided in the robust summary was obtained from the OECD document for adipic acid (<http://cs3-hq.oecd.org/scripts/hpv/>).

**NOAEL = 750 mg/kg-bw/day**

**LOAEL = 2250 mg/kg-bw/day** (based on decreased body weight gain)

### ***Reproductive Toxicity***

Although reproductive studies were not performed, no evidence of toxicity was noted in reproductive organs during the two-year feeding study described above.

### ***Developmental Toxicity***

#### ***Adipic acid (CASRN 124-04-9; supporting chemical)***

(1) In a developmental toxicity study, groups of 20-24 pregnant Wistar rats were administered adipic acid via oral gavage at doses of 0, 2.9, 13.0, 62.0 or 288 mg/kg-day on gestation days (GD) 6-15. Body weights were recorded on GD 0, 6, 11, 15 and 20. All dams were subjected to caesarian section on GD 20 and evaluated for urogenital tract abnormalities; the numbers of implantation/resorption sites and viable/non-viable offspring were recorded. One third of each litter was examined for soft-tissue abnormalities and the remaining animals were evaluated for skeletal defects. No treatment-related embryotoxic, teratogenic or maternal effects were observed in this study.

**Maternal/Developmental NOAEL = 288 mg/kg-day** (based on no observed adverse effects at the highest dose tested)

(2) In a developmental toxicity study, groups of 10-14 pregnant Dutch-belted rabbits were administered adipic acid via oral gavage at doses of 0, 2.5, 12.0, 54.0 or 250 mg/kg-day on gestation days (GD) 6-18. Body weights were recorded on GD 0, 6, 12, 18 and 29. All dams were subjected to caesarian section on GD 29 and evaluated for urogenital tract abnormalities; the numbers of corpora lutea, implantation/resorption sites and viable/non-viable offspring were recorded. Each fetus was examined for external abnormalities. Body weights were recorded for live pups and these animals were subsequently maintained in an incubator for 24 hours to evaluate treatment-related effects on neonatal survival. All surviving pups were sacrificed and examined for visceral/skeletal abnormalities. No treatment-related embryotoxic, teratogenic or maternal effects were observed in this study.

**Maternal/Developmental NOAEL = 250 mg/kg-day** (based on no observed adverse effects at the highest dose tested)

### ***Genetic Toxicity – Gene Mutation***

#### ***In vitro***

*Salmonella typhimurium* strains TA1535, TA1537, TA98 and TA100 and *Escherichia coli* strain WP2 uvrA were exposed to cyclohexane, oxidized, aqueous extract dissolved in dimethyl

sulfoxide (DMSO) with and without metabolic activation at 0 (solvent control), 40, 200, 1000, 5000 or 10,000 µg/plate. The cytotoxic concentration was  $\geq 5000$  µg/plate. Positive controls were tested concurrently, but no information on control response was provided.

**Cyclohexane, oxidized, aqueous extract was not mutagenic in this assay.**

#### *Genetic Toxicity – Chromosomal Aberrations*

##### *In vivo*

A micronucleus assay was conducted in male NMR1 mice (5/dose). Cyclohexane, oxidized, aqueous extract (emulsified in corn oil) was administered via oral gavage at doses of 0, 500, 1000 or 2000 mg/kg-bw/day once per day for two days. Cyclophosphamide (20 mg/kg-bw) was used as a positive control. Animals were sacrificed 24 hours after the last dose and the number of micronuclei/2000 polychromatic erythrocytes was counted. Negative and positive controls responded appropriately in this assay. No statistically significant increases in micronuclei were observed following exposure to cyclohexane, oxidized, aqueous extract.

**Cyclohexane, oxidized, aqueous extract did not induce chromosomal aberrations in this assay.**

#### *Additional Information*

##### *Skin Irritation*

###### *Adipic acid (CASRN 124-04-9; supporting chemical)*

Six male albino rabbits (strain not specified) were administered 0.5 g adipic acid paste (50% (wt/wt) of the test material in propylene glycol) via dermal exposure for 24 hours under semi-occlusive conditions. Slight to mild irritation was observed in 3/6 rabbits 24 hours after application to intact skin. No other details were provided in the robust summary.

**Adipic acid was minimally irritating to rabbit skin in this assay.**

##### *Eye Irritation*

###### *Adipic acid (CASRN 124-04-9; supporting chemical)*

Two albino rabbits (strain, sex not specified) received 10 mg of adipic acid via topical application to the right conjunctival sac. Twenty seconds after contact, the treated eye of one rabbit was washed with tap water for one minute, while the treated eye of the other rabbit was left unwashed. Minimal irritation of the iris and conjunctiva occurred following treatment; however, treatment effects resolved within 3 and 14 days in the washed and unwashed eyes, respectively.

**Adipic acid was minimally irritating to rabbit eye in this assay.**

**Conclusion:** The acute oral toxicity of CASRN 68915-38-8 is low; the oral LD<sub>50</sub> is  $> 5000$  mg/kg-day in rats. Genotoxicity studies represent the only other health hazard data that is available for the sponsored chemical. CASRN 124-04-9 is one of the most abundant carboxylic acid components in CASRN 68915-38-8. Although EPA agrees that use of CASRN 124-04-9 as a supporting chemical for CASRN 68915-38-9 may be reasonable, there are other pending issues. A two-year feeding study conducted with CASRN 124-04-9 revealed significant

decreases in body weight gain in male rats treated at doses of 2250 mg/kg-bw/day or higher; however, there was no overall effect on body weight. The NOAEL for systemic toxicity is 750 mg/kg-bw/day (based on dose-related decreases in body weight gain). Prenatal developmental toxicity studies with CASRN 124-04-9 showed no treatment-related maternal or developmental effects following oral gavage at the highest dose tested in rats (288 mg/kg-day) or rabbits (250 mg/kg-day). Reproductive studies were not performed; however, an evaluation of reproductive organs in the two-year feeding study described above did not show any evidence of toxicity in reproductive tissues (testes, ovaries and uteri). Both skin and eye irritation were observed following topical application of CASRN 124-04-9 in rabbits. CASRN 124-04-9 did not induce gene mutations *in vitro* or chromosomal aberrations *in vivo*. CASRN 124-04-9 may be a reasonable choice for supporting chemical given the likely metabolism of 6-hydroxycaproic acid (CASRN 1191-25-9) to CASRN 124-04-9; however, EPA believes that *in vitro* studies documenting the rate of metabolic conversion are warranted, given uncertainties regarding the reaction kinetics associated with aldehyde formation.

#### 4. Hazards to the Environment

The environmental hazard data are summarized in Table 4.

##### *Acute Toxicity to Fish*

Golden orfe (*Leuciscus idus L.*) were exposed to cyclohexane, oxidized, aqueous extract at nominal concentrations of 0, 100, 215, 464, or 1000 mg/L under static conditions for 96 hours. The pH for the control group was approximately 7.9 and ranged from 4.2 to 7.7 for the treatment groups with a concentration-dependent decrease. Mortality was 100% at 464 and 1000 mg/L by 48 hours. No mortality was seen at lower concentrations. No mortality occurred when the pH of a 1000 mg/L test solution was adjusted to 7.3 prior to initiation of the 96-hour exposure.

**96-h LC<sub>50</sub> = 316 mg/L**

##### *Acute Toxicity to Aquatic Invertebrates*

Water fleas (*Daphnia magna*) were exposed to cyclohexane, oxidized, aqueous extract at nominal concentrations of 0, 12.5, 25, 50 or 100 mg/L under static conditions for 48 hours. Concentrations measured for 12.5 and 100 mg/L at 48 hours and were within 100 to 150% of the nominal concentrations. Daphnid swimming ability was not affected at any concentration tested.

**48-h EC<sub>50</sub> > 100 mg/L**

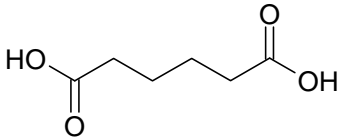
##### *Toxicity to Aquatic Plants*

Green algae (*Desmodesmus subspicatus*) were exposed to cyclohexane, oxidized, aqueous extract at nominal concentrations of 0, 5, 10, 22, 50, and 100 mg/L under static conditions for 72 hours. At test initiation, the analytically determined concentrations of the test substance in the test water were in the range of 83-93% in the three highest concentrations.

**72-h EC<sub>50</sub> (growth) > 100 mg/L**

**72-h EC<sub>50</sub> (biomass) = 92 mg/L**

**Conclusion:** The measured 96-hour LC<sub>50</sub> of CASRN 68915-38-8 to fish is 316 mg/L. The measured 48-hour EC<sub>50</sub> of CASRN 68915-38-8 to aquatic invertebrates is >100 mg/L. The measured 72-hour EC<sub>50</sub> of CASRN 68915-38-8 to aquatic plants is >100 mg/L for growth and 92 mg/L for biomass.

<b>Table 4. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program</b>		
<b>Endpoints</b>	<b>SUPPORTING CHEMICAL</b>  <b>Adipic acid</b> <b>(CASRN 124-04-9)</b> (Component of CASRN 68915-38-8 and supporting chemical for mixture)	<b>SPONSORED CHEMICAL</b>  <b>Cyclohexane, oxidized, aq. ext.</b> <b>(CASRN 68915-38-8)</b>
<b>Structural Formula</b>		<b>Complex Mixture</b>
<b>Summary of Human Health Data</b>		
<b>Acute Oral Toxicity</b> <b>LD<sub>50</sub> (mg/kg-bw)</b>		<b>&gt; 5000</b>
<b>Repeated-Dose Toxicity</b> <b>NOAEL/LOAEL</b> <b>Oral (mg/kg-bw/day)</b>	<b>NOAEL = 750</b> <b>LOAEL = 2250</b>	Data gap
<b>Developmental Toxicity</b> <b>NOAEL/LOAEL</b> <b>Oral (mg/kg-bw/day)</b>	<b>NOAEL = 288 (hdt)</b> (Maternal and Developmental)	Data gap
<b>Reproductive Toxicity</b>	Evaluation of reproductive organs in the two-year bioassay coupled with the developmental toxicity studies meet the HPV Challenge requirement for this endpoint.	Data gap
<b>Genetic Toxicity –</b> <b>Gene Mutation</b> <i>In vitro</i>		<b>Negative</b>
<b>Genetic Toxicity –</b> <b>Chromosomal Aberrations</b> <i>In vivo</i>		<b>Negative</b>

<b>Table 4. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program</b>		
	<b>SUPPORTING CHEMICAL</b>	<b>SPONSORED CHEMICAL</b>
<b>Endpoints</b>	<b>Adipic acid (CASRN 124-04-9)</b> (Component of CASRN 68915-38-8 and supporting chemical for mixture)	<b>Cyclohexane, oxidized, aq. ext. (CASRN 68915-38-8)</b>
<b>Additional Information</b>		
<b>Dermal Irritation</b>	<b>Minimal</b>	No Data
<b>Eye Irritation</b>	<b>Minimal</b>	
<b>Summary of Environmental Effects – Aquatic Toxicity Data</b>		
<b>Fish</b>		
<b>96-h LC<sub>50</sub> (mg/L)</b>		<b>316</b>
<b>Aquatic Invertebrates</b>		
<b>48-h EC<sub>50</sub> (mg/L)</b>		<b>&gt; 100</b>
<b>Aquatic Plants</b>		
<b>72-h EC<sub>50</sub> (mg/L) (growth/biomass)</b>		<b>&gt;100 / 92</b>

Measured data in bold text; (RA) = Read Across; hdt = highest dose tested