

## SCREENING-LEVEL HAZARD CHARACTERIZATION

### Dechlorane Plus<sup>®</sup> (CASRN 13560-89-9)

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.

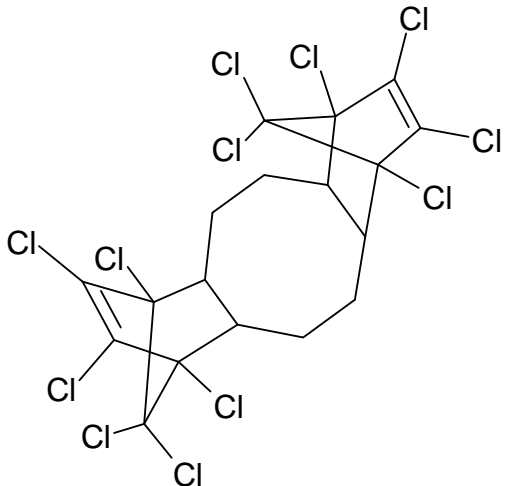
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<sup>1</sup> U.S. EPA. High Production Volume (HPV) Challenge Program; <http://www.epa.gov/chemrtk/index.htm>.

<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 provide information previously not readily available to the public.

<p><b>Chemical Abstract Service Registry Number (CASRN)</b></p>	<p><b>13560-89-9</b></p>
<p><b>Chemical Abstract Index Name</b></p>	<p><b>1,4:7,10-Dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro-]</b></p>
<p><b>Structural Formula</b></p>	

**Summary**

CASRN 13560-89-9 is a white, crystalline powder possessing negligible vapor pressure and negligible water solubility. It is expected to possess low mobility in soil. Volatilization is considered moderate based on its Henry's Law constant. The rate of hydrolysis is negligible. The rate of atmospheric photooxidation is moderate. CASRN 13560-89-9 is expected to have high persistence (P3) and high bioaccumulation potential (B3).

The acute toxicity of CASRN 13560-89-9 is low in rats and rabbits, via the oral and dermal routes, respectively. The acute inhalation toxicity is moderate in rats. A 28-day repeated-dose toxicity study in rats via gavage showed no treatment-related effects; the NOAEL for systemic toxicity is 5000 mg/kg-day (highest dose tested). A 28-day inhalation toxicity study in rats showed effects on liver (increased absolute liver weight, hepatocytomegaly of centrilobular hepatocytes in males at and above 0.64 mg/L-day and in females at 1.52 mg/L-day) and effects on the lungs (increased absolute lung weights and increased number of macrophages in alveoli

in females at 0.64 mg/L-day and in males at both concentrations—only two concentrations tested). The LOAEC for systemic toxicity is 0.64 mg/L-day; the NOAEC was not established. A 28-day dermal toxicity study in rabbits showed statistically significant decreases in absolute and relative liver and ovarian weights in females at 500 and 2000 mg/kg-day (only two doses tested); however, there were no corresponding histopathological findings. The NOAEL is 2000 mg/kg-day (highest dose tested). In a combined oral repeated-dose/reproductive/developmental toxicity screening test in rats no effects on reproductive or developmental parameters were seen at 5000 mg/kg-day (highest dose tested). The NOAEL for reproductive, maternal and developmental toxicity is 5000 mg/kg-day. CASRN 13560-89-9 did not induce gene mutations in bacteria or mammalian cells *in vitro*. No adequate data were provided for the chromosomal aberrations endpoint. CASRN 13560-89-9 was not irritating to rabbit eyes.

No adequate data are available on the sponsored substance. Based on the low water solubility (0.0002 mg/L; measured) and high log  $K_{ow}$  values (11.3; estimated) of CASRN 13560-89-9, acute and chronic aquatic toxicity are not expected.

The genetic toxicity (chromosomal aberrations) endpoint was identified as a data gap under the HPV Challenge Program.

The sponsor, Occidental Chemical Corporation (OxyChem), submitted a Test Plan and Robust Summaries to EPA for Dechlorane Plus<sup>®</sup> (CASRN 13560-89-9; CA index name: 1,4:7,10-dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro-) on September 24, 2004. EPA posted the submission on the ChemRTK HPV Challenge website on November 2, 2004 (<http://www.epa.gov/chemrtk/pubs/summaries/dechlorp/c15635tc.htm>). EPA comments on the original submission were posted to the website on August 16, 2005. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents dated May 9, 2005, December 20, 2006 and March 3, 2009 which were posted to the ChemRTK website on June 7, 2005, February 2, 2007 and June 8, 2009, respectively.

## **1. Chemical Identity**

### **1.1 Identification and Purity**

The physical-chemical properties of 1,4:7,10-dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro- are summarized in Table 1.

### **1.2 Physical-Chemical Properties**

1,4:7,10-Dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro- is a white, crystalline powder possessing negligible vapor pressure and negligible water solubility. It exists as a combination of both the syn and anti-isomers.

<b>Table 1. Physical-Chemical Properties of 1,4:7,10-Dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro-<sup>1</sup></b>	
<b>Property</b>	<b>Value</b>
CASRN	13560-89-9
Molecular Weight	653.73
Physical State	White, crystalline powder
Melting Point	Decomposes at 350°C (measured)
Boiling Point	Decomposes at 350°C without boiling (measured)
Vapor Pressure	0.006 mm Hg at 200°C (measured); <1×10 <sup>-10</sup> mm Hg at 25°C (estimated) <sup>2</sup>
Water Solubility	2.49×10 <sup>-4</sup> mg/L at 25°C (measured); 4.4×10 <sup>-5</sup> mg/L at 22°C (measured)
Dissociation Constant (pK <sub>a</sub> )	Not applicable
Henry's Law Constant	7.5×10 <sup>-6</sup> atm-m <sup>3</sup> /mol (estimated) <sup>2</sup>
Log K <sub>ow</sub>	11.3 (estimated) <sup>2</sup>

<sup>1</sup>Occidental Chemical Company. 2009. Revised Test Plan and Robust Summary for Dechlorane Plus. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/dechlorp/c15635tc.htm> as of January 6, 2011.

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

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

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

CASRN 13560-89-9 had an aggregated production and/or import volume in the United States between one million pounds and ten million pounds during calendar year 2005.

Non-confidential information in the IUR indicated that the industrial processing and uses for the chemical include flame retardants. Non-confidential commercial and consumer uses of this chemical include electrical and electronic products.

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

The environmental fate properties of 1,4:7,10-dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro- are summarized in Table 2.

1,4:7,10-Dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro- is expected to possess low mobility in soil. 1,4:7,10-Dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro-, present at 100 mg/L, achieved 0.6% of its theoretical biochemical oxygen demand (BOD) in 2 weeks using an activated sludge inoculum at

30 mg/L and the modified MITI (OECD 301C) test. It was also not readily biodegradable in separate aerobic biodegradation studies using sewage sludge as inocula, and it did not degrade in 2–6 weeks in sewage sludge inoculum maintained under anaerobic conditions. The rate of hydrolysis is negligible. The rate of volatilization is considered moderate based on its Henry's Law constant; however, the rate of volatilization may be attenuated by the tendency to adsorb to soil and sediment. 1,4:7,10-Dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro- had bioconcentration factors (BCF) of 14 – 212 measured in carp and was determined to be non or not highly bioaccumulative due to its low water solubility; however, recent studies in highly contaminated areas of China and South Korea, where this compound has been used for over 4 decades, suggests that this substance is bioaccumulative and biomagnifies in the food chain. Both syn- and anti- isomers of 1,4:7,10-dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro- were significantly biomagnified in the food web, with trophic magnification factors (TMFs) of 11.3 and 6.6, respectively. The trophic magnification potentials of the both isomers were generally comparable to or lower than those of the highly recalcitrant PCB congeners in the same food web, but were 2-3 times greater than those of PBDE congeners. Dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro- is expected to have high persistence (P3) and high bioaccumulation potential (B3).

**Conclusion:** 1,4:7,10-Dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro- is a white, crystalline powder possessing negligible vapor pressure and negligible water solubility. It is expected to possess low mobility in soil. Volatilization is considered moderate based on its Henry's Law constant. The rate of hydrolysis is negligible. The rate of atmospheric photooxidation is moderate. 1,4:7,10-Dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro- is expected to have high persistence (P3) and high bioaccumulation potential (B3).

<b>Table 2. Environmental Fate Characteristics of 1,4:7,10-Dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro-1</b>	
<b>Property</b>	<b>Value</b>
Photodegradation Half-life	5.6 hours (estimated) <sup>2</sup>
Hydrolysis Half-life	Stable
Biodegradation	0% after 21 days (not readily biodegradable); 0% after 14 days (not readily biodegradable); No biodegradation after 2–6 weeks under anaerobic conditions; 0.6% after 14 days (not readily biodegradable) <sup>3</sup>
Bioaccumulation Factor	BCF = 1.97–7.02 (measured in bluegills) <sup>8</sup> ; BCF = 23–121 (measured in carp at 0.0027 mg/L) <sup>3</sup> ; BCF = 14–96 (measured in carp at 0.00027 mg/L) <sup>3</sup> ; BAF = 2.3×10 <sup>4</sup> (estimated) <sup>2</sup> ; Studies in contaminated industrial locations of China and South Korea indicated this substance is bioaccumulative and bioavailable. Both syn- and anti-dechlorane plus were significantly biomagnified in the food web, with trophic magnification factors (TMFs) of 11.3 and 6.6, respectively. <sup>4,5</sup> Biomagnification factors of 5.2 (syn-isomer) and 1.9 (anti-isomer) measured in rainbow trout <sup>6</sup>
Log K <sub>oc</sub>	7.7 (estimated) <sup>2</sup>
Fugacity (Level III Model) <sup>2</sup>	Air (%) <0.1 Water (%) 5.1 Soil (%) 91.5 Sediment (%) 3.4
Persistence <sup>7</sup>	P3 (high)
Bioaccumulation <sup>7</sup>	B3 (high)

<sup>1</sup> Occidental Chemical Company. 2009. Revised Test Plan and Robust Summary for Dechlorane Plus. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/dechlorp/c15635tc.htm> as of January 6, 2011.

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

<sup>3</sup> National Institute of Technology and Evaluation. 2002. Biodegradation and Bioaccumulation of the Existing Chemical Substances under the Chemical Substances Control Law. Available online at [http://www.safe.nite.go.jp/english/kizon/KIZON\\_start\\_hazkizon.html](http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html) as of July 14, 2010.

<sup>4</sup> Wu JP, Zhang Y, Luo XJ, Wang J, Chen SJ, Guan YT, Mai BX. 2010. Isomer-specific bioaccumulation and trophic transfer of Dechlorane Plus in the freshwater food web from a highly contaminated site, South China. *Environ. Sci. Technol.* 44(2):606-11

<sup>5</sup> Kang JH, Kim JC, Jin GZ, Park H, Baek SY, Chang YS. 2010. Detection of Dechlorane Plus in Fish from Urban Industrial Rivers. *Chemosphere* 79: 850-854.

<sup>6</sup> Tomy GT, Thomas CR, Zidane TM, Murison KE, Pleskach K, Hare J, Arsenault G, Marvin CH, Sverko E. 2008. Examination of Isomer Specific Bioaccumulation Parameters and Potential in vivo Hepatic Metabolites of syn- and anti- Dechlorane Plus Isomers in Juvenile Rainbow Trout (*Oncorhynchus mykiss*). *Environ. Sci. Technol.* 42: 5562-5567.

<sup>7</sup> Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

<sup>8</sup> The bioaccumulation potential has conflicting evidence regarding the degree of bioaccumulation, however, the most recent data suggests a high potential to bioaccumulate. Moreover, one isomer (syn-isomer) appears to bioaccumulate to a greater extent than the anti-isomer. Monitoring data and bioaccumulation studies suggest that bioaccumulation and biomagnification may occur in the environment although measured BCF values are relatively low.

### 3. Human Health Hazard

A summary of health effects data submitted for SIDS endpoints is provided in Table 3. The table also indicates where data for the supporting chemical are read-across (RA) to the sponsored chemical.

#### *Acute Oral Toxicity*

(1) Sherman-Wistar rats (3 males and 2 females/dose) were administered CASRN 13560-89-9 (~ 99% pure) via gavage at 1500, 3000, 6000, 12,500 or 25,000 mg/kg and observed for up to 14 days following dosing. There were no mortalities.

**LD<sub>50</sub> > 25,000 mg/kg**

(2) Sprague-Dawley rats (2 males/dose) were administered CASRN 13560-89-9 (~ 99% pure) via gavage at 10, 31.6, 100, 316, 1000 or 3160 mg/kg- and observed for up to 48 hours following dosing. There were no mortalities.

**LD<sub>50</sub> > 3160 mg/kg**

#### *Acute Inhalation Toxicity*

Rats (5/sex; strain unspecified) were exposed to CASRN 13560-89-9 (~ 99% pure) as dust via inhalation at a nominal concentration of 2.25 mg/L for 4 hours and observed for up to 14 days following exposure. There were no mortalities.

**LC<sub>50</sub> > 2.25 mg/L**

#### *Acute Dermal Toxicity*

Albino rabbits (4/dose, sex and strain not specified) were administered CASRN 13560-89-9 (~ 99% pure) via the dermal route at 500, 1000, 2000, 4000 or 8000 mg/kg- to shaved intact or abraded skin under unspecified conditions. Observation period was not indicated. There were no mortalities.

**LD<sub>50</sub> > 8000 mg/kg**

#### *Repeated-Dose Toxicity*

(1) Rats (15/sex/dose; strain unspecified) were administered CASRN 13560-89-9 (~99% pure) in the diet at 0, 10,000, 30,000 and 100,000 ppm (0, ~500, 1500 and 5000 mg/kg-day, respectively) for 13 weeks. Mortality and adverse effects were recorded daily and body weights and food consumption were recorded weekly. Blood and urine samples were collected at approximately 45 and 84 days after treatment initiation for blood chemistry and hematology parameters and urinalyses evaluations. Necropsies were performed on all rats and the brain, gonads, heart, kidneys, liver and spleen of each animal were weighed. Thirty tissues and organs were collected for histopathological examination. There were no statistically-significant treatment-related effects on body or organ weights, urinalysis, clinical chemistry, or hematology. There were no treatment-related clinical signs or gross pathological or histopathological findings. Food consumption was slightly higher in high-dose females, but this parameter was not analyzed statistically. Absolute and relative liver weights were increased in high-dose males. Although

these increases were outside the normal range for the laboratory, they were not statistically significant nor were there any associated histopathological lesions.

**NOAEL = 5000 mg/kg-day** (highest dose tested)

(2) In a combined repeated-dose/reproductive/developmental toxicity screening test, Crl:CD (SD) rats (10/sex/dose) were administered CASRN 13560-89-9 (~99% pure) in corn oil via gavage at 750, 1500 or 5000 mg/kg-day, daily, for 28 days. [Although a total of 30 rats/sex/dose were included in the study, 10 rats/sex/dose were assigned for the repeated-dose toxicity phase.] Blood and urine samples for clinical pathology evaluations (hematology, coagulation, clinical chemistry, and urinalysis) were collected at termination. Animals were necropsied the day following termination of dosing. Organ weights were recorded and selected tissues were microscopically examined. No treatment-related effects were observed on clinical signs of toxicity, body weights, food consumption, neurobehavioral and functional observational battery evaluations. In addition, no effects were observed on hematology, urinalysis, coagulation or clinical chemistry parameters, and no changes in organ weights were observed. Mortality observed across all dose groups (1/30, 2/30, 2/30, 2/30 for males and 2/30, 3/30, 1/30, and 2/30 for females at control, 750, 1500 and 5000 mg/kg-day, respectively) was accompanied by gross and microscopic evidence of gavage errors (perforations of the esophagus, trachea and white fluid in lung). Microscopic lesions observed in the thoracic or pleural cavities consisted of adhesions, inflammation and fibrosis with evidence of esophageal perforations noted in some animals. In addition, microscopic findings were observed that were associated with an antigenic stimulus, immune response and/or a physiological stress response secondary to the presence of test material in the thoracic cavity. These findings were not dose-dependent and were observed in animals with evidence of suspected gavage injury.

**NOAEL = 5000 mg/kg-day** (highest dose tested)

(3) COBS rats (5/sex/dose) were exposed to CASRN 13560-89-9 dust (~99% pure) via inhalation at 0.64 or 1.524 mg/L for 6 hours/day, 5 days/week for 28 days. Mortality and other adverse effects were recorded daily and body weights were recorded just prior to initiation of the study and weekly thereafter. Blood and urine samples were collected prior to initiation of exposure and at the end of the exposure period. Necropsies were performed on all animals and the brain, gonads, heart, kidneys, liver, lungs and spleen of each animal were weighed. At least 12 tissues and organs were collected for histopathological examination. There were no treatment-related effects on body weights, signs of toxicity, urinalysis, hematology and clinical chemistry parameters, or gross pathology. Male and female rats of both exposure groups had significantly increased absolute liver weights compared to controls, with corresponding hepatocytomegaly of centrilobular hepatocytes in males at both concentrations and in 2 of 5 females at 1.524 mg/L-day. Females at 0.64 mg/L-day and males and females at 1.524 mg/L-day had significantly increased absolute lung weights compared to controls. Slightly increased numbers of macrophages in the alveoli were observed in all exposed male and female rats. There were no other exposure-related effects observed.

**LOAEC = 0.64 mg/L-day** (based on increased absolute liver weight, hepatocytomegaly of centrilobular hepatocytes, increased absolute lung weights, increased numbers of macrophages in alveoli)

**NOAEC = Not established**

(4) New Zealand White rabbits (5/sex/dose) were administered CASRN 13560-89-9 (~99% pure) in 3% aqueous methylcellulose at 0 (untreated control), 500 or 2000 mg/kg-day via the dermal route for 5 days/week for 4 weeks. The test substance was distributed over ~20% of the total body surface area on shaved abraded skin. The application sites were not occluded; the animals were fitted with Elizabethan collars throughout the study to reduce ingestion of the test material. Mortality and adverse effects were recorded daily and body weights were measured weekly. Food consumption was not measured. Blood and urine samples were collected from 2 animals/sex/dose on day 6 and day 23 for evaluation of blood chemistry and hematology parameters and urinalyses. Necropsies were performed on all rats and the brain, gonads, heart, kidneys, liver, thyroids, adrenals and spleen of each animal were weighed. Approximately thirty tissues and organs were collected for histopathological examination. The only treatment-related clinical sign was minimal erythema at the application site. There were no treatment-related effects on body weights, urinalysis, hematology, clinical chemistry, gross pathology or histopathology. Females exhibited statistically significant, dose-related decreases in absolute and relative (to body and brain weight) liver and ovarian weights; however, no corresponding histopathology was observed in these organs.

**NOAEL = 2000 mg/kg-day** (highest dose tested)

### ***Reproductive/Developmental Toxicity***

In a combined repeated-dose/reproductive/developmental toxicity screening test, Crl:CD (SD) rats (30/sex/dose) were administered CASRN 13560-89-9 (~99% pure) in corn oil via gavage at 750, 1500 or 5000 mg/kg-day for 63 days in males and 43-64 days in females. For the reproductive/developmental toxicity phase, 20 rats/sex/dose were used. Following a 21-day pre-mating period, males and females of the same treatment group were paired for mating. On gestation day 20, selected females were euthanized and subjected to a complete necropsy, including a uterine examination in which the total number of implantations, early and late resorptions, viable and nonviable fetuses, the position of the cervix, gravid uterine weights and total number of corpora lutea were recorded. All fetuses were weighed, sexed, examined externally and processed for visceral examination. Malformations and developmental variations were recorded. All surviving mated females not selected for euthanasia on gestation day 20 were allowed to give birth. Observations of the F1 offspring included survival at birth and through lactation day 4, and individual pup body weights and clinical observations on lactation day 0 and 4. On lactation day 4, surviving pups and dams were euthanized and subjected to necropsy. At termination of the study, surviving males were euthanized and subjected to necropsy; additionally, selected male organ weights were recorded. No treatment-related effects were observed on the reproductive (estrous cyclicity, reproduction, and fertility indices) or developmental (parturition, gestation length, litter size, implantations, pup body weights, sex ratios and fetal external and visceral malformations or variations) parameters evaluated in this study. Mortalities (3-5 animals out of 30) were observed across all dose groups, including controls. Mortalities were associated with pathological (gross and microscopic) evidence of gavage errors (perforations of the esophagus, trachea and white fluid in lung).

**NOAEL (reproductive toxicity) = 5000 mg/kg-day** (highest dose tested)

**NOAEL (maternal/developmental toxicity) = 5000 mg/kg-day** (highest dose tested)

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

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

(1) *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to CASRN 13560-89-9 (~99% pure) in dimethylsulfoxide (DMSO) at concentrations of 0, 50, 100, 500, 1000, 5000 or 10,000 µg/plate with and without metabolic activation. Positive and solvent controls were tested concurrently and responded appropriately. No cytotoxicity or increases in number of revertants were observed.

**CASRN 13560-89-9 did not induce gene mutations in this assay.**

(2) Mouse lymphoma cells heterozygous at the thymidine kinase (T/K) locus were exposed to CASRN 13560-89-9 (~99% pure) at concentrations of 1 – 50 µg/mL with and without metabolic activation. Positive controls were tested concurrently and responded appropriately. Precipitate was observed at 30 – 50 µg/mL in unactivated cells and 20 – 50 µg/mL in activated cells. No cytotoxicity was observed at concentrations of 1 – 20 µg/mL and no increases in mutation frequencies were noted.

**CASRN 13560-89-9 did not induce gene mutations in this assay.**

### ***Genetic Toxicity – Chromosomal Aberrations***

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

No adequate data are available for this endpoint.

### ***Additional Information***

#### ***Eye Irritation***

Undiluted CASRN 13560-89-9 (0.1 mL; ~ 99% pure) was instilled in the conjunctival sac of the right eyes of 9 rabbits (3/group). The other eyes served as controls. Test eyes were not rinsed in one group or were rinsed 2 or 4 seconds following the test substance instillation in two additional groups. Irritation was scored up to 3 days after administration. No corneal, iridal or conjunctival effects were observed.

**CASRN 13560-89-9 was not irritating to rabbit eyes in this study.**

**Conclusion:** The acute toxicity of CASRN 13560-89-9 is low in rats and rabbits, via the oral and dermal routes, respectively. The acute inhalation toxicity is moderate in rats. A 28-day repeated-dose toxicity study in rats via gavage showed no treatment-related effects; the NOAEL for systemic toxicity is 5000 mg/kg-day (highest dose tested). A 28-day inhalation toxicity study in rats showed effects on liver (increased absolute liver weight, hepatocytomegaly of centrilobular hepatocytes in males at and above 0.64 mg/L-day and in females at 1.52 mg/L-day) and effects on the lungs (increased absolute lung weights and increased number of macrophages in alveoli in females at 0.64 mg/L and in males at both concentrations—only two concentrations tested). The LOAEC for systemic toxicity is 0.64 mg/L-day; the NOAEC was not established. A 28-day dermal toxicity study in rabbits showed statistically significant decreases in absolute and relative liver and ovarian weights in females at 500 and 2000 mg/kg-day (only two doses

tested); however, there were no corresponding histopathological findings. The NOAEL is 2000 mg/kg-day (highest dose tested). In a combined oral repeated-dose/reproductive/developmental toxicity screening test in rats no effects on reproductive or developmental parameters were seen at 5000 mg/kg-day (highest dose tested). The NOAEL for reproductive, maternal and developmental toxicity is 5000 mg/kg-day. CASRN 13560-89-9 did not induce gene mutations in bacteria or mammalian cells *in vitro*. No adequate data were provided for the chromosomal aberrations endpoint. CASRN 13560-89-9 was not irritating to rabbit eyes.

<b>Table 3. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data</b>	
<b>Endpoints</b>	<b>SPONSORED CHEMICAL Dechlorane Plus<sup>®</sup> (13560-89-9)</b>
<b>Acute Toxicity Oral LD<sub>50</sub> (mg/kg)</b>	<b>&gt; 25,000</b>
<b>Acute Toxicity Inhalation LC<sub>50</sub> (mg/L)</b>	<b>&gt; 2.25</b>
<b>Acute Toxicity Dermal LD<sub>50</sub> (mg/kg)</b>	<b>&gt; 8000</b>
<b>Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-day)</b>	<b>NOAEL = 5000 (highest dose tested)</b>
<b>Repeated-Dose Toxicity NOAEC/LOAEC Inhalation (mg/L-day)</b>	<b>NOAEC = Not established LOAEC = 0.64</b>
<b>Repeated-Dose Toxicity NOAEL/LOAEL Dermal (mg/kg-day)</b>	<b>NOAEL = 2000 (highest dose tested)</b>
<b>Reproductive/Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)</b>	
<b>Reproductive Toxicity</b>	<b>NOAEL = 5000 (highest dose tested)</b>
<b>Maternal/Developmental Toxicity</b>	<b>NOAEL = 5000 (highest dose tested)</b>
<b>Genetic Toxicity -Gene Mutation <i>In vitro</i></b>	<b>Negative</b>
<b>Genetic Toxicity - Chromosomal Aberrations</b>	<b>Data Gap</b>
<b>Additional Information Eye Irritation</b>	<b>Not Irritating</b>

#### 4. **Hazard to the Environment**

##### *Acute Toxicity to Fish, Aquatic Invertebrates and Toxicity to Aquatic Plants*

The submitted fish acute study reported an LC<sub>50</sub> value for CASRN 13560-89-9 of >100 mg/L and tested above the measured water solubility of 0.0002 mg/L. Neither acute nor chronic aquatic invertebrate nor aquatic plant studies were submitted for CASRN 13560-89-9. Due to the high estimated log K<sub>ow</sub> (11.3) and low measured water solubility, EPA believes acute and chronic toxicity will not be observed for CASRN 13560-89-9.

**Conclusion:** No adequate data are available on the sponsored substance. Based on the low water solubility (0.0002 mg/L; measured) and high log K<sub>ow</sub> values (11.3; estimated) of CASRN 13560-89-9, acute and chronic aquatic toxicity are not expected.