

## SCREENING-LEVEL HAZARD CHARACTERIZATION

### SPONSORED CHEMICAL

**1,3-Butanediol**      **CASRN 107-88-0**

### SUPPORTING CHEMICALS

**1,4-Butanediol**      **CASRN 110-63-4**

**1,2-Butanediol**      **CASRN 584-03-2**

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

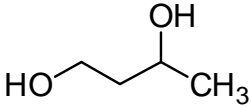
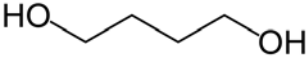
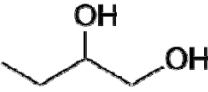
<sup>1</sup> U.S. EPA. High Production Volume (HPV) Challenge Program; <http://www.epa.gov/chemrtk/index.htm>.

<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>.

authorities around the world. OPPT is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments.

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

<p><b>Chemical Abstract Service Registry Number (CASRN)</b></p>	<p><b><u>Sponsored Chemical</u></b> <b>107-88-0</b></p> <p><b><u>Supporting Chemicals</u></b> <b>110-63-4</b> <b>584-03-2</b></p>
<p><b>Chemical Abstract Index Name</b></p>	<p><b><u>Sponsored Chemical</u></b> <b>1,3-Butanediol</b></p> <p><b><u>Supporting Chemicals</u></b> <b>1,4-Butanediol</b> <b>1,2-Butanediol</b></p>
<p><b>Structural Formula</b></p>	<p><b><u>Sponsored Chemical</u></b></p>  <p><b><u>Supporting Chemicals</u></b></p>  
<p style="text-align: center;"><b>Summary</b></p> <p>CASRN 107-88-0 is a clear, viscous liquid with high water solubility and moderate vapor pressure. It is expected to possess high mobility in soil. Volatilization is expected to be low based upon the estimated Henry's Law constant. Hydrolysis of CASRN 107-88-0 is negligible. The rate of atmospheric photooxidation is considered moderate. CASRN 107-88-0 is expected to have low persistence (P1) and low bioaccumulation potential (B1).</p> <p>The acute oral toxicity of CASRN 107-88-0 is low in rats. A 13-week feeding study with CASRN 107-88-0 in dogs showed decreased body weight, increased (relative) liver and kidney weights and increased seizure activity at 9000 mg/kg-bw/day; the NOAEL for systemic toxicity is 6000 mg/kg-bw-day. Two chronic feeding studies with CASRN 107-88-0 showed no treatment-related effects in rats or dogs following two years of dietary exposure; the NOAELs for systemic toxicity are 6230 and 7300 mg/kg-bw/day (highest doses tested) in male and</p>	

female rats, respectively and 589 mg/kg-bw/day (highest dose tested) in dogs. In a five-generation reproductive toxicity study with CASRN 107-88-0 in rats, decreased fertility was observed in treated dams following dietary exposure at 20,200 mg/kg-bw/day during successive (third, fourth and fifth) mating cycles; the NOAEL for reproductive toxicity is 7360 mg/kg-bw/day. A significant increase in skeletal anomalies (incomplete skeletal ossification) was observed in pups born to dams treated at concentrations  $\geq$  8420 mg/kg-bw/day; the NOAEL for developmental toxicity is 4120 mg/kg-bw/day. In a prenatal oral gavage developmental toxicity study in rats, maternal sedation and decreased pup weight were observed at 4236 and 7060 mg/kg-day, respectively; the NOAELs for maternal and developmental toxicity are 706 and 4236 mg/kg-day, respectively. The supporting chemical, CASRN 110-63-4 did not induce gene mutations in bacterial cells *in vitro*. CASRN 107-88-0 did not induce chromosomal aberrations in rat bone marrow cells *in vivo*. No evidence of carcinogenic activity was observed during a two-year feeding study with CASRN 107-88-0 in rats.

The acute 96-h LC<sub>50</sub> value for fish for the supporting chemical, CASRN 584-03-2, is 1000 mg/L. The acute 48-h EC<sub>50</sub> value for aquatic invertebrates for the supporting chemical, CASRN 584-03-2, is >1000 mg/L. The 72-h EC<sub>50</sub> value for aquatic plants for CASRN 107-88-0 is >1070 mg/L (growth rate).

No data gaps were identified under the HPV Challenge Program.

The sponsor, Celanese Ltd., submitted a Test Plan and Robust Summaries to EPA for 1,3-Butanediol (CASRN 107-88-0; CA Index name: 1,3-butanediol) on December 18, 2002. EPA posted the submission on the ChemRTK HPV Challenge website on January 15, 2003 (<http://www.epa.gov/oppt/chemrtk/pubs/summaries/13butane/c14133tc.htm>). EPA comments on the original submission were posted to the website on May 13, 2003. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on July 15, 2003, which were posted to the ChemRTK website on August 6, 2003.

### **Justification for Supporting Chemical**

The sponsor proposed use of 1,4-butanediol (CASRN 110-63-4) as a supporting chemical for the gene mutation, acute toxicity to fish and acute toxicity to aquatic invertebrates endpoints. EPA accepted the use of CASRN 110-63-4 as a supporting chemical for the gene mutation endpoint based on structural similarities with the sponsored chemical, 1,3-butanediol (CASRN 107-88-0). The sponsor provided aquatic toxicity data for 1,4-butanediol (CASRN 110-63-4), 1,2-butanediol (CASRN 584-03-2), 1,2-propanediol (CASRN 57-55-6), and 1, 2-ethanediol (CASRN 107-21-1) to demonstrate comparable toxicities. CASRN 584-03-2 is listed as a SIDS chemical. Aquatic toxicity data for this analog were used to support the sponsored chemical. This information can be found at <http://www.chem.unep.ch/irptc/sids/OECDSIDS/584032.pdf>. EPA agrees that the use of data for the supporting chemical, CASRN 584-03-2, is justified based on structural similarities. Data submitted for CASRNs 57-55-6, 107-21-1 and 110-63-4 are not used to address aquatic toxicity endpoints in this hazard characterization.

## **1. Chemical Identity**

### **1.1 Identification and Purity**

CASRN 107-88-0 is a diol used as a chemical intermediate in the manufacture of polyester plasticizers and other products.

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

CASRN 107-88-0 is a clear, viscous liquid with high water solubility and moderate vapor pressure. The physical-chemical properties of CASRN 107-88-0 are summarized in Table 1.

<b>Property</b>	<b>Value</b>
CASRN	107-88-0
Molecular Weight	90.12
Physical State	Clear, viscous liquid
Melting Point	-77°C (measured)
Boiling Point	207.5°C (measured)
Vapor Pressure	0.06 mm Hg at 20°C (measured) 0.0201 mm Hg at 25°C (measured)
Water Solubility	Miscible
Dissociation Constant (pK <sub>a</sub> )	Not applicable
Henry's Law Constant	2.4×10 <sup>-9</sup> atm·m <sup>3</sup> /mole (calculated) <sup>2</sup>
Log K <sub>ow</sub>	-0.29 (estimated) <sup>2</sup>

**Table 1. Physical-Chemical Properties of 1,3-Butanediol<sup>1</sup>**

<b>Property</b>	<b>Value</b>
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<sup>1</sup> Celanese Ltd. 2003. Revised Test Plan and Robust Summary for 1,3-Butanediol. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/13butane/c14133tc.htm> as of July 9, 2010.

<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 June 28, 2010.

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

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

CASRN 107-88-0 had an aggregated production and/or import volume in the United States between 10 and 50 million pounds during calendar year 2005.

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include other basic organic chemical manufacturing as intermediates; and paint and coating manufacturing. Non-confidential commercial and consumer uses of this chemical include paints and coatings; soaps and detergents; and “other.”

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

The environmental fate characteristics of the sponsored chemical are summarized in Table 2.

CASRN 107-88-0 is expected to possess high mobility in soil. CASRN 107-88-0 was found to be readily biodegradable (80.5% degradation in 28 days) using a modified Sturm test (OECD 301B). The rate of hydrolysis is expected to be negligible since CASRN 107-88-0 does not contain functional groups that are susceptible to hydrolysis under environmental conditions. The rate of volatilization is expected to be low based on the estimated Henry’s Law constant. CASRN 107-88-0 is expected to have low persistence (P1) and low bioaccumulation potential (B1).

<b>Property</b>	<b>Value</b>
Photodegradation Half-life	9 hours (estimated) <sup>2</sup>
Hydrolysis Half-life	Stable
Biodegradation	80.5% after 28 days (readily biodegradable)
Bioaccumulation Factor	BAF = 0.9 (estimated) <sup>2</sup>
Log K <sub>oc</sub>	<0.001 (estimated) <sup>2</sup>
Fugacity (Level III Model) <sup>2</sup>	
Air (%)	0.1
Water (%)	33.7
Soil (%)	66.1
Sediment (%)	0.1
Persistence <sup>3</sup>	P1 (low)
Bioaccumulation <sup>3</sup>	B1 (low)

<sup>1</sup> Celanese Ltd. 2003. Revised Test Plan and Robust Summary for 1,3-Butanediol. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/13butane/c14133tc.htm> as of July 9, 2010.

<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 June 28, 2010.

<sup>3</sup> Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

**Conclusion:** CASRN 107-88-0 is a clear, viscous liquid with high water solubility and moderate vapor pressure. It is expected to possess high mobility in soil. Volatilization is expected to be low based upon the estimated Henry's law constant. Hydrolysis of 1 CASRN 107-88-0 is negligible. The rate of atmospheric photooxidation is considered moderate. CASRN 107-88-0 is expected to have low persistence (P1) and low bioaccumulation potential (B1).

### **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***

##### ***1,3-Butanediol (CASRN 107-88-0)***

Rats (strain, sex, number not specified) were administered CASRN 107-88-0 (purity not stated) via the oral route at unspecified concentrations and observed for 14 days.

**LD<sub>50</sub> = 22,800 mg/kg**

#### ***Acute Inhalation Toxicity***

##### ***1,3-Butanediol (CASRN 107-88-0)***

Rats (strain, sex and number not specified) were administered CASRN 107-88-0 (purity not stated) via vapor inhalation at approximately 60 ppm (~ 0.22 mg/L) for 8 hours. No mortalities were observed. No information on the length of observation was provided.

**LC<sub>50</sub> > 0.22 mg/L**

### ***Repeated-Dose Toxicity***

#### ***1,3-Butanediol (CASRN 107-88-0)***

(1) Weanling Sprague-Dawley rats (30/sex/dose; 60/sex in control group) were administered CASRN 107-88-0 (purity 99.98%) in the diet at 1, 3 or 10% (~ 643, 1960 or 6230 mg/kg-bw/day for males or ~ 844, 2330 or 7300 mg/kg-bw/day for females) for two years. Blood and urine samples were collected from each treatment group at six time intervals for determination of hematology (complete blood count, hematocrit and hemoglobin) and urinalysis measurements (acetone, pH, protein, specific gravity, glucose, urobilinogen and occult blood). Ten animals from each dose group were necropsied after one year on test. Representative organ weights (liver, kidney, adrenal, thyroid and testes) were recorded and 17 organs (type not specified) were submitted for histopathologic evaluation. This procedure was repeated with surviving animals after two years of dietary exposure to CASRN 107-88-0. No treatment-related effects on mortality, body weight gain, organ weights, hematology, histopathology or neoplastic changes were observed in this study.

**NOAEL (males) ~ 6230 mg/kg-bw/day** (highest dose tested)

**NOAEL (females) ~ 7300 mg/kg-bw/day** (highest dose tested)

(2) Beagle dogs (4/sex/group) were administered CASRN 107-88-0 (purity 99.98%) in the diet at 0, 0.5, 1 or 3% (~ 98, 196 or 589 mg/kg-bw/day) for two years. Blood and urine samples were collected from each treatment group at eight time intervals for determination of hematology (complete blood count, hematocrit, hemoglobin, sedimentation rate and blood urea nitrogen) and urinalysis measurements (acetone, pH, protein, specific gravity, glucose, urobilinogen and occult blood). A liver function test (bromsulphalein retention method) was also conducted using control and treated animals. Four animals from each dose group (2/sex) were necropsied after one year on test. Representative organ weights (liver, kidney, adrenal, thyroid and testes) were recorded and 19 organs (type not specified) were submitted for a complete histopathology evaluation. No treatment-related effects on mortality, body weight gain, organ weights, hematology, liver function, histopathology or neoplastic changes were observed following two years of dietary exposure to CASRN 107-88-0.

**NOAEL ~ 589 mg/kg-bw/day** (highest dose tested)

(3) Beagle dogs (4/sex/group) were administered CASRN 107-88-0 (purity 99.5%) in the diet at 0, 3000, 6000, 9000 or 12,000 mg/kg-bw/day for 13 weeks. Animals were evaluated regularly for changes in behavior, general health, body weight and food consumption. Evaluations of hematology measurements (hemoglobin, methemoglobin, packed cell volume, Heinz bodies and erythrocyte, reticulocyte and total/differential leukocyte counts), clinical chemistry parameters (serum glutamate pyruvate transaminase, serum alkaline phosphatase, total serum protein, serum albumin, fasting blood glucose, blood urea nitrogen, triglycerides, free fatty acids,  $\beta$ -hydroxybutyric acid, acetoacetic acid, and lactate) and urinalysis (specific gravity, pH, glucose, protein, occult blood, ketones and microscopic examination of the sediment) were conducted on all animals at 0, 6 and 12 weeks on test. In addition, liver (bromsulphophthalein method) and kidney function (phenol red excretion method) were evaluated in all control and high-dose animals at study completion (week 13). Organ weights (heart, kidneys, liver, spleen, lungs, testicles/ovaries, pituitary, thyroid, adrenals and brain) were recorded at necropsy and samples taken from these and other tissues (spinal cord, sciatic nerve, salivary glands, skeletal muscle, thoracic aorta, skin, tonsils, bladder, esophagus, stomach, duodenum, jejunum, ileum, caecum,

colon, pancreas, trachea, circumanal glands, eyes, epididymis, prostate, uterus, gall bladder, tongue and thymus) were fixed and stained for microscopic examination. Decreased body weight and increased (relative) organ weights (liver and kidney) and hematology measures (platelet counts and serum glutamate pyruvate transaminase) were observed at 9000 and 12,000 mg/kg-bw/day. Other effects noted at the highest dose (12,000 mg/kg-bw/day) included slight ketonuria and changes in organ weights (increased relative brain, adrenal and lung weights; decreased relative thymus and spleen weights) and clinical chemistry parameters ( $\gamma$ -hydroxybutyric acid, acetoacetic acid, lactate, methemoglobin, serum glutamic-oxaloacetic transaminase). The only statistically significant finding reported in the robust summary was a dose-related increase in free fatty acids in animals treated at 12,000 mg/kg-bw/day. Study authors stated that the biological significance of epileptic seizures observed at or above 9000 mg/kg-bw/day was unknown, as idiopathic epilepsy was commonly seen in this animal colony.  
**LOAEL = 9000 mg/kg-bw/day** (based on reduced body weight, clinical chemistry changes, increased relative liver and kidney weights and an increased incidence of epileptic seizures)  
**NOAEL = 6000 mg/kg-bw/day**

### ***Reproductive Toxicity***

#### ***1,3-Butanediol (CASRN 107-88-0)***

In a five-generation reproductive toxicity study lasting 77 weeks, Wistar rats (25/sex/group) were administered CASRN 107-88-0 (purity not specified) in the diet at 0, 5, 10 or 24% (~ 0, 3680, 7360 or 17,700 mg/kg-bw/day for males or ~ 0, 4120, 8420 or 20,200 mg/kg-bw/day for females). After four weeks on the respective diets, rats were paired for mating. Treated females received CASRN 107-88-0 throughout mating, gestation and lactation. Reproductive parameters (pregnancy rate, litter size, pup weight and survival) were evaluated for each litter. All F0 females were allowed to deliver normally. The initial litters were raised to maturity. After 11 weeks on test, 25 F1 males and 25 F1 females were randomly selected from each treatment group and paired to produce the F2 generation. Subsequent generations were reared to maturity and subjected to successive reproduction cycles. Five successive mating cycles were achieved within a period of 77 weeks. Reproductive parameters for each cycle were evaluated as previously described for the F0 generation. In addition, the gonads and pituitary glands of F1 rats which survived at least 66 weeks were evaluated for microscopic abnormalities. No significant treatment-related effects were observed upon histopathologic examination of the testes, ovaries or pituitary glands. Reproductive and lactation parameters were comparable among control and treated groups for four of five successive generations; however, the pregnancy rate of control and treated rats decreased during five successive mating cycles. No offspring were produced at the highest dose in the fifth generation. No significant differences in pup weight or survival were observed between control and treated groups; however, incomplete skeletal ossification was observed in pups born to dams treated at  $\geq 8420$  mg/kg-bw/day.

**LOAEL (reproductive toxicity) ~ 17,700mg/kg-bw/day** (based on impaired fertility)

**NOAEL (reproductive toxicity) ~ 7360 mg/kg-bw/day**

**LOAEL (developmental toxicity) ~ 8420 mg/kg-bw/day** (based on incomplete skeletal ossification in pups)

**NOAEL (developmental toxicity) ~ 4120 mg/kg-bw/day**

## ***Developmental Toxicity***

### ***1,3-Butanediol (CASRN 107-88-0)***

In a prenatal developmental toxicity screening test, pregnant Long-Evans rats (10 females/dose) received CASRN 107-88-0 (98% purity) as an aqueous solution via gavage administration at 706, 4236 or 7060 mg/kg-day on gestation days (GD) 6 – 15. Animals were monitored daily for clinical signs of intoxication (lethargy, ataxia) and mortality. All dams were sacrificed on GD 20 and offspring were delivered by caesarean section. At necropsy, total uterine weight, total litter weight, individual pup weights, crown-rump length, number of live pups, stillbirths, number of resorptions and implantation sites, sex distribution and number of corpora lutea were recorded for each pregnancy. Live pups were examined for gross malformations at birth. Maternal sedation was observed at concentrations  $\geq$  4236 mg/kg-day. Other treatment-related effects observed in this study included a significant decrease in pup weights at 7060 mg/kg-day (highest dose tested). Study authors noted that this effect was only observed in male offspring that were not contiguous *in utero* to a female sibling. No maternal mortality was observed. No treatment-related effects on dam body weight gain, corpora lutea or total litter weight were observed. No other treatment effects were reported in this study.

**LOAEL (maternal toxicity) = 4236 mg/kg-day** (based on sedation)

**NOAEL (maternal toxicity) = 706 mg/kg-day**

**LOAEL (developmental toxicity) = 7060 mg/kg-day** (based on decreased pup weight)

**NOAEL (developmental toxicity) = 4236 mg/kg-day**

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

### ***In vitro***

#### ***1,4-Butanediol (CASRN 110-63-4, supporting chemical)***

*Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 and *Escherichia coli* strain WP2 uvrA were exposed to CASRN 110-63-0 (98% purity) at 0, 313, 625, 1250 or 5000  $\mu$ g/plate with and without metabolic activation. No cytotoxicity was observed in any of the strains at the highest concentration tested (5000  $\mu$ g/plate) with or without metabolic activation. Information regarding control responses was not provided.

**CASRN 110-63-4 was not mutagenic in this assay.**

### ***In vivo***

#### ***1,3-Butanediol (CASRN 107-88-0)***

In a dominant lethal assay, Wistar rats (10 males/group) were administered CASRN 107-88-0 (purity not specified) in the diet at 0, 5, 10 or 24% (~ 3680, 7360 or 17,700 mg/kg-bw/day) for 13 weeks. Males were then mated to virgin untreated females each week for 8 consecutive weeks. Upon removal from the mating cage, females were housed individually for seven days and then sacrificed for examination of the reproductive tract. The numbers of implantation and/or resorption sites and viable/dead offspring were recorded. These data were used to calculate the mutagenic index. The mutagenic index (number of resorptions as a percentage of implant sites) showed no positive trend with increasing concentrations of CASRN 107-88-0 in the diet.

**CASRN 107-88-0 was not mutagenic in this assay.**

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

### ***In vivo***

#### ***1,3-Butanediol (CASRN 107-88-0)***

In a cytogenetic assay, Wistar rats ( $\geq 2$ /sex/group) were administered CASRN 107-88-0 (purity not specified) in the diet at 0, 5, 10 or 24% ( $\sim 3680$ , 7360 or 17,700 mg/kg-bw/day for males or  $\sim 4120$ , 8420 or 20,200 mg/kg-bw/day for females) for 13 weeks. Bone marrow preparations were examined cytologically for treatment-related aberrations in the chromosomal patterns. The frequency of occurrence of abnormal cells was determined to be within the normal range, therefore specific aberrations were not reported. No information was provided regarding control responses.

**CASRN 107-88-0 did not induce chromosomal aberrations in this assay.**

### ***Additional Information***

#### ***Carcinogenicity***

#### ***1,3-Butanediol (CASRN 107-88-0)***

In the two-year oral repeated-dose study described previously, no increase in tumor incidence was observed in Sprague-Dawley rats following dietary exposure to CASRN 107-88-0.

**CASRN 107-88-0 was not carcinogenic to rats in this study.**

**Conclusion:** The acute oral toxicity of CASRN 107-88-0 is low in rats. A 13-week feeding study with CASRN 107-88-0 in dogs showed decreased body weight, increased (relative) liver and kidney weights and increased seizure activity at 9000 mg/kg-bw/day; the NOAEL for systemic toxicity is 6000 mg/kg-bw-day. Two chronic feeding studies with CASRN 107-88-0 showed no treatment-related effects in rats or dogs following two years of dietary exposure; the NOAELs for systemic toxicity are 6230 and 7300 mg/kg-bw/day (highest doses tested) in male and female rats, respectively and 589 mg/kg-bw/day (highest dose tested) in dogs. In a five-generation reproductive toxicity study with CASRN 107-88-0 in rats, decreased fertility was observed in treated dams following dietary exposure at 20,200 mg/kg-bw/day during successive (third, fourth and fifth) mating cycles; the NOAEL for reproductive toxicity is 7360 mg/kg-bw/day. A significant increase in skeletal anomalies (incomplete skeletal ossification) was observed in pups born to dams treated at concentrations  $\geq 8420$  mg/kg-bw/day; the NOAEL for developmental toxicity is 4120 mg/kg-bw/day. In a prenatal oral gavage developmental toxicity study in rats, maternal sedation and decreased pup weight were observed at 4236 and 7060 mg/kg-day, respectively; the NOAELs for maternal and developmental toxicity are 706 and 4236 mg/kg-day, respectively. The supporting chemical, CASRN 110-63-4 did not induce gene mutations in bacterial cells *in vitro*. CASRN 107-88-0 did not induce chromosomal aberrations in rat bone marrow cells *in vivo*. No evidence of carcinogenic activity was observed during a two-year feeding study with CASRN 107-88-0 in rats.

<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 1,3-Butanediol (107-88-0)</b>	<b>SUPPORTING CHEMICAL 1,4-Butanediol (110-63-4)</b>
<b>Acute Toxicity Oral LD<sub>50</sub> (mg/kg)</b>	<b>22,800</b>	<b>-</b>
<b>Acute Toxicity Inhalation LC<sub>50</sub> (mg/L)</b>	<b>&gt; 0.22</b>	<b>-</b>
<b>Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)</b>	<b>(rats) NOAEL ~ 6230 (m; highest dose tested) NOAEL ~ 7300 (f; highest dose tested)  (dogs) NOAEL ~ 589 (highest dose tested) NOAEL = 6000 LOAEL = 9000</b>	<b>-</b>
<b>Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)</b>	<b>Reproductive  NOAEL ~ 7,360 LOAEL ~ 17,700  Developmental  NOAEL~ 4120 LOAEL ~ 8420</b>	<b>-</b>
<b>Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-day)</b>	<b>Maternal  LOAEL = 4236 NOAEL = 706  Developmental  NOAEL = 4236 LOAEL = 7060</b>	<b>-</b>
<b>Genetic Toxicity - Gene Mutation <i>In vitro</i></b>	<b>No Data Negative (RA)</b>	<b>Negative</b>
<b>Genetic Toxicity - Chromosome Aberrations <i>In vivo</i></b>	<b>Negative</b>	<b>-</b>

<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 1,3-Butanediol (107-88-0)</b>	<b>SUPPORTING CHEMICAL 1,4-Butanediol (110-63-4)</b>
<b>Additional Information Carcinogenicity</b>	<b>Negative</b>	<b>-</b>

Measured data in bold; (RA) = read across; - endpoint not addressed for this chemical

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

A summary of aquatic toxicity data submitted for SIDs endpoints is provided in Table 4. The table also indicates where data for the supporting chemical are read-across (RA) to the sponsored chemical.

##### ***Acute Toxicity to Fish***

###### ***1,2-Butanediol (CASRN 584-03-2, supporting chemical)***

Data for CASRN 584-03-2 that were used to assess this endpoint can be found at <http://www.chem.unep.ch/irptc/sids/OECDSEIDS/584032.pdf>.

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

###### ***1,2-Butanediol (CASRN 584-03-2, supporting chemical)***

Data for CASRN 584-03-2 that were used to assess this endpoint can be found at <http://www.chem.unep.ch/irptc/sids/OECDSEIDS/584032.pdf>.

**48-h EC<sub>50</sub> = 2895 mg/L** (estimated using ECOSAR version 1.00a)

##### ***Toxicity to Aquatic Plants***

###### ***1,3-Butanediol (CASRN 107-88-0)***

Green algae (*Pseudokirchneriella subcapitata*) were exposed to CASRN 107-88-0 at the nominal concentration of 1000 mg/L for 72 hours. The mean measured concentration was 1070 mg/L. 1,3-Butanediol did not inhibit growth of algae.

**72-h EC<sub>50</sub> (growth) = > 1070 mg/L**

**Conclusion:** The acute 96-h LC<sub>50</sub> value for fish for the supporting chemical, CASRN 584-03-2, is 1000 mg/L. The acute 48-h EC<sub>50</sub> value for aquatic invertebrates for the supporting chemical, CASRN 584-03-2, is >1000 mg/L. The 72-h EC<sub>50</sub> value for aquatic plants for CASRN 107-88-0 is >1070 mg/L (growth rate).

<b>Table 4. Summary of the Screening Information Data Set under the U.S. HPV Challenge Program - Aquatic Toxicity Data</b>		
<b>Endpoints</b>	<b>SPONSORED CHEMICAL 1,3-Butanediol (107-88-0)</b>	<b>SUPPORTING CHEMICAL 1,2-Butanediol (584-03-2)</b>
<b>Fish 96-h LC<sub>50</sub> (mg/L)</b>	No Data 1000 (RA)	<b>1000 (24-h)</b>
<b>Aquatic Invertebrates 48-h EC<sub>50</sub> (mg/L)</b>	No Data >1000 (RA)	<b>&gt;1000 (24-h) 2895(e)</b>
<b>Aquatic Plants 72-h EC<sub>50</sub> (mg/L) growth</b>	<b>&gt;1070</b>	-

**bold = measured data** (i.e., derived from testing); (e) = ECOSAR value (version 1.00a); (RA) = read across; - indicates endpoint not addressed for this chemical