

## **SCREENING-LEVEL HAZARD CHARACTERIZATION**

### **Pyrolysis C3+ and Pyrolysis C4+ Category**

#### **SPONSORED CHEMICALS**

**(See Table 1)**

#### **SUPPORTING CHEMICALS**

**(See Table 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, EXTTOXNET, 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

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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>.

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.

<b>Category Name</b>	<b>Pyrolysis C3+ and Pyrolysis C4+ Category</b>
<b>Chemical Abstract Service Registry Number (CASRN)</b>	<p align="center"><b><u>Sponsored Chemicals</u></b> See Table 1</p> <p align="center"><b><u>Supporting Chemicals</u></b> See Table 2</p>
<b>Chemical Abstract Index Name</b>	<p align="center"><b><u>Sponsored Chemicals</u></b> See Table 1</p> <p align="center"><b><u>Supporting Chemicals</u></b> See Table 2</p>
<b>Structural Formula</b>	<p align="center"><b><u>Sponsored Chemicals</u></b> See representative structures in Appendix</p> <p align="center"><b><u>Supporting Chemicals</u></b> See representative structures in Appendix</p>
<p align="center"><b>Summary</b></p> <p>Pyrolysis C3+ and Pyrolysis C4+ are intermediate streams in the ethylene process and consist of the portions of the liquefied cracked gas remaining after removal of ethane and lighter components (for the C3+ stream) or removal of propane and lighter (in the case of the C4+ stream). These streams consist of a complex mixture of hydrocarbons. The substances of this category are gasses possessing high vapor pressure and moderate water solubility. All category members are expected to possess high mobility in soil. Volatilization is expected to be high. The rate of hydrolysis is expected to be negligible. The rate of atmospheric photooxidation is expected to be slow to rapid for the members of this category. The members of the pyrolysis C3+ and pyrolysis C4+ category are expected to possess low persistence (P1) and low bioaccumulation potential (B1).</p> <p>Since the category substances are gases, the major route of exposure to humans is via inhalation. Therefore all human health endpoints have been evaluated using the inhalation route of exposure.</p> <p>For pyrolysis C3+ and pyrolysis C4+ category members, the acute oral and inhalation toxicity in rats is low and moderate, respectively, and acute dermal toxicity in rabbits is low based on supporting chemicals' data. The supporting chemical, CASRN 68955-28-2, is not irritating to rabbit skin or eyes.</p> <p>Repeated-exposure studies with the supporting chemical, CASRN 71-43-2 show that the hematopoietic system is the most sensitive indicator of toxicity. Mice exposed repeatedly for 13 weeks via vapor inhalation to CASRN 71-43-2, showed hematological effects [e.g. decreases in RBC and WBC counts, platelets, hemoglobin, hematocrit], thymic atrophy and testicular effects at 0.96 mg/L/day; the NOAEC for systemic toxicity is 0.1 mg/L/day. In a similar study in mice, designed to assess specific effects on hematology, exposure to CASRN 71-43-2 for 10 weeks resulted in increases in spleen weight, total nucleated cells per spleen and nucleated RBCs at 0.03 mg/L/day; the NOAEC is not established. Repeated inhalation exposure of rats to CASRN</p>	

71-43-2 showed a decrease in WBC counts and percentage of lymphocytes at 0.96 mg/L/day; the NOAEC for hematological effects on peripheral blood circulation is 0.096 mg/L/day. The NOAEC for repeated exposure to the supporting chemical, CASRN 106-99-0, gas to mice for 13 weeks, is 625 ppm/day based on mortality seen at 1250 ppm/day. In a 13-week repeated-exposure study with CASRN 106-99-0 gas, rats showed no adverse effects at the highest concentration tested; NOAEC for systemic toxicity is 8000 ppm/day (highest concentration tested).

Guideline reproductive toxicity studies are not available for CASRN 71-43-2; however, in the 13-week inhalation exposures in mice, adverse effects were observed on the male and female reproductive organs. The sperm head morphology assay in mice for the supporting chemical, CASRN 106-99-0 (administered as gas), showed concentration-related increases in the percentage of abnormal sperm heads following five days of inhalation exposure to gas at concentrations of 200 to 5000 ppm. A 5-day inhalation exposure to CASRN 106-99-0, supporting chemical (gas), to male mice (mated with untreated females) in the dominant lethal test caused increases in the number of dead implantations (early) at concentrations as low as 200 ppm; although a strict concentration-response relationship was not observed. In the longer-term (4-weeks) dominant lethal test, inhalation exposure of CASRN 106-99-0, supporting chemical (gas) to male mice (mated with untreated female mice) showed early deaths at 65 ppm; the NOAEC is 12.5 ppm.

In the prenatal developmental toxicity study in mice via inhalation (gas), the supporting chemical, CASRN 106-99-0 showed decreased maternal body weight gains and decreased fetal and placental weights with an increased incidence of fetal variations at and above 200 ppm; the NOAEC is 40 ppm. Rats showed maternal and developmental toxicity when exposed to CASRN 106-99-0 gas via inhalation at 200 ppm based on decreased maternal body weight gains and fetal growth retardation, respectively; the NOAEC is not established. In the prenatal developmental toxicity study via gavage, the supporting chemical CASRN 64741-74-8 caused abortions in rabbit does at 50 mg/kg-day; the NOAEL for maternal toxicity is 25 mg/kg-day and for developmental toxicity it is 50 mg/kg-day (highest dose tested).

CASRN 71-43-2 induced gene mutations in bacteria and sister chromatid exchange in human lymphocytes *in vitro* and in rat and mouse lymphocytes *in vivo*. CASRN 71-43-2 induced micronuclei in rats and mice *in vivo*. The supporting chemical, CASRN 68955-28-2, was mutagenic in mammalian cells *in vitro* (but was not mutagenic in bacteria), induced chromosomal aberrations *in vivo* and induced unscheduled DNA synthesis *in vitro*. The supporting chemical, CASRN 68476-52-8, induced chromosomal aberrations *in vivo*. The supporting chemical, CASRN 106-99-0, was mutagenic in bacteria *in vitro* and induced chromosomal aberrations *in vivo*. The supporting chemical, CASRN 64741-74-8, was not mutagenic in bacteria *in vitro*; however, it was mutagenic in mammalian cells *in vitro* and caused DNA damage in bacteria in a DNA repair assay *in vitro*.

The supporting chemical, CASRN 71-43-2, is a known human carcinogen for all routes of exposure. The supporting chemical, CASRN 106-99-0, increased incidences of various tumors at multiple sites in rats and mice and there is “sufficient evidence” from epidemiologic studies of exposed workers to consider CASRN 106-99-0 carcinogenic to humans.

Based on the supporting chemicals, the 96-h LC<sub>50</sub> for fish is 4.26 mg/L (CASRN 109-66-0), the 48-h EC<sub>50</sub> for aquatic invertebrates is 2.7 mg/L (CASRN 109-66-0), and the 72-h EC<sub>50</sub> for aquatic plants ranges from 7.5 (CASRN 513-35-9) to 40 mg/L (CASRN 74-85-1) for biomass and 10.7 (CASRN 109-66-0) to 72 mg/L (CASRN 74-85-1) for growth rate. The chronic 32-d NOEC fish toxicity value is 0.8 mg/L (CASRN 71-43-2).

No data gaps were identified under the HPV Challenge Program.

The sponsor, ACC Olefins Panel, submitted a Test Plan and Robust Summaries to EPA for the Crude Butadiene C4 category on May 4, 2000. EPA posted the submission on the ChemRTK HPV Challenge website on May 19, 2000 (<http://www.epa.gov/oppt/chemrtk/pubs/summaries/olefins/c12064tc.htm>). EPA comments on the original submission were posted to the website on September 13, 2000. The sponsor submitted updated/revised documents on August 1, 2002, October 14, 2003, May 4, 2004 and May 17, 2005, which were posted to the ChemRTK website on August 20, 2002, December 1, 2003, August 26, 2004 and June 10, 2005, respectively.

**Category Identification/Justification**

The Pyrolysis C3+ and Pyrolysis C4+ Category streams arise from production processes associated with ethylene manufacturing (see Appendix for a description of the ethylene and associated processes—as presented in the test plan). In its original test plan, the sponsor grouped four production streams associated with ethylene manufacturing with 11 CASRNs into the crude butadiene C4 category. In its revised test plans, however, the sponsor separated them into two categories with two streams each: (1) crude butadiene C4 streams category and (2) pyrolysis C3+ and pyrolysis C4+ streams category. This hazard characterization pertains to the pyrolysis C3+ and pyrolysis C4+ category. A separate hazard characterization has been prepared for crude C4 butadiene category.

The revised Pyrolysis C3+ and Pyrolysis C4+ category contains intermediate streams from the ethylene manufacturing process (Table 1) and consist of the portions of the liquefied cracked gas remaining after removal of ethane and lighter components (for the C3+ stream) or removal of propane and lighter (in the case of the C4+ stream). The two commercial production streams, Pyrolysis C3+ and Pyrolysis C4+, are similar from a process and toxicology perspective. Each stream can vary in composition, not only between manufacturers but also for an individual manufacturer, depending on feedstock type and process operating conditions. These streams consist of a complex mixture of hydrocarbons with the typical carbon (C) number distribution ranges predominantly between C3 and C10, but can include beyond C12.

<b>Streams</b>	<b>CASRN</b>	<b>Name</b>
Pyrolysis C3+	64742-83-2 68513-68-8	Naphtha, petroleum, light steam-cracked Residues, petroleum, deethanizer tower
Pyrolysis C4+	64742-83-2	Naphtha, petroleum, light steam-cracked

Please note: The TSCA Chemical Substance Inventory definitions for the CASRNs in this category can be vague with respect to composition. Therefore, it is not uncommon that a CASRN is correctly used to describe different streams (different compositions) or that two or more CASRNs are used to describe one stream (similar composition or process). For this reason, the data matrix for this category are developed based on two compositionally differentiated process streams, rather than on the CASRNs in this category.

1,3-Butadiene (CASRN 106-99-0) and benzene (CASRN 71-43-2) are the predominant constituents of these streams (Table 3). Much of the data used to characterize the hazard for this category are from 1,3-butadiene and benzene because they are the most reactive constituents and thus presumed to be more biologically active components contributing to toxicity of the streams. 1,3-Butadiene and benzene can be present in the two streams at concentrations between approximately 12 to 42% and 11 to 42% (by weight), respectively; thus, they can represent from 23 to 84% of the total (by weight) composition. This commonality was the basis for considering the two streams as a category for purposes of the HPV Challenge Program.

### **Justification for Supporting Chemicals**

The supporting chemicals are listed in Table 2. For the purposes of hazard characterization, data for 1,3-butadiene and 1,3-butadiene-containing streams as identified in the crude butadiene C4 category (<http://www.epa.gov/chemrtk/pubs/summaries/olefins/c12064tc.htm>) and for benzene and benzene-containing streams as identified in the high benzene naphthas category (<http://www.epa.gov/chemrtk/pubs/summaries/hibenznp/c13436tc.htm>) are used to address human health effects endpoints because as stated above, these chemicals represent from 23 to 84% of the total (by weight) stream composition. 1,3-Butadiene and benzene are the most biologically active among all the constituents in the pyrolysis C3+ and pyrolysis C4+ streams category; therefore, these chemicals and the selected streams containing them are considered to be adequate supporting chemicals. 1,3-Butadiene has been assessed at SIAM 4 in the OECD HPV Program; ([http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/butadienereport019.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/butadienereport019.pdf)) and benzene has been assessed at SIAM 21 in the OECD HPV Program; ([http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf)). EPA IRIS assessments are also available for benzene (CASRN 71-43-2: <http://www.epa.gov/ncea/iris/subst/0276.htm>) and 1,3-butadiene (CASRN 106-99-0: <http://www.epa.gov/ncea/iris/subst/0139.htm>).

For aquatic toxicity, the sponsor indicated that measured data on aquatic toxicity endpoints are not available and instead submitted ECOSAR data on the chemical constituents in the category. Also, the sponsor included the aquatic toxicity values of several chemicals from the High Benzene Naphthas Category without robust summary in the test plan. EPA determined that the measured data from ethylene (CASRN 74-85-1), pentane (CASRN 109-66-0) 2-butene, 2-methyl- (CASRN 513-35-9), and benzene (CASRN 71-43-2) are appropriate to support this category based on their similar physico-chemical properties, environmental fate and mode of toxic action (narcosis). In addition, these chemicals are used to set boundaries and cover the low and high carbon numbers in the category (C3-C6). Therefore, data from these supporting chemicals can adequately characterize the aquatic toxicity hazard for this category. These supporting chemicals have been assessed at OECD SIAMs under the OECD HPV program: ethylene (SIAM 5; <http://www.chem.unep.ch/irptc/sids/OECDIDS/74851.pdf>); pentane (SIAM 13; [http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/n-pentanereport043.pdf](http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/n-pentanereport043.pdf)), 2-butene, 2-methyl-(SIAM 19; <http://www.chem.unep.ch/irptc/sids/OECDIDS/513359.pdf>), and benzene

[http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf).

<b>Table 2. Supporting Chemicals for Human Health Endpoints</b>	
CASRN	Name
<i>C4 Crude Butadiene Category</i>	
68955-28-2	Gases, (petroleum) light steam cracked, butadiene conc.
68476-52-8	Hydrocarbons, C4, ethylene manufactured by-product
106-99-0	1,3-Butadiene
<i>High Benzenes Naphthas Category</i>	
No CASRN	Pyrolysis gasoline stream (dripolene)
68410-97-9	Hydrotreated C6 – 8 fraction (hydrogenated pyrolysis gasoline)
71-43-2	Benzene
64741-74-8	C5 – 10 Fraction pyrolysis gasoline (rerun tower overheads)
<b>Supporting Chemicals for Environmental Effects Endpoints</b>	
74-85-1	Ethylene
109-66-0	Pentane
513-35-9	2-Butene, 2-methyl-

<b>Table 3. Typical Constituent (wt%) Range of Streams in the Pyrolysis C3+ and Pyrolysis C4+ Category (as presented in the sponsor's test plan)</b>	
<b>Constituent</b>	<b>Pyrolysis C3+ and Pyrolysis C4+ Streams (wt %)</b>
Propylene	0 - 4.0
Other C3 & Lighter Hydrocarbons	0 - 1.0
Isobutane	0.0 - 1.1
Isobutylene	5.0 - 12
n-Butane	1.0 - 4.5
cis- & trans-Butene-2	1.5 - 6.4
Butene-1	5.0 - 11
1,3-Butadiene	12 - 42
1,2-Butadiene	0.0 - 1.0
1,4-Pentadiene	0.2 - 1.2
Pentene-1	0.5 - 2.3
2-Methyl-1,3-Butadiene (Isoprene)	0.6 - 3.2
cis- & trans-Pentene-2	0.1 - 2.0
1,3-Cyclopentadiene	1.0 - 9.5
cis- & trans-1,3-Pentadiene	1.0 - 7.2
Cyclopentene	0.5 - 2.6
Cyclopentane	2.0 - 4.0
C6-C8 Non-Aromatic Hydrocarbons	2.0 - 12
Benzene	11 -42
Toluene	1.8 - 25
Xylenes	0.1 - 4.0
Ethylbenzene	0.1 - 1.3
Other C9+ Hydrocarbons	1.5 - 8.7
Dicyclopentadiene	2.0 - 10
Indene	0.3 - 1.9
Naphthalene	0.2 - 1.6

Note 1: The composition of category streams as listed in Table 2 do not represent all possible constituents, but rather those that were reported by the manufacturers. The balance of these streams is expected to be other hydrocarbons that have boiling points in the range of the listed components.

Note 2: The listed ranges should not be considered absolute values. They are instead the approximate highs and lows of the reported values, and are expected to be typical limit values.

## **1. Chemical Identity**

### **1.1 Identification and Purity**

For supporting chemicals/streams, the robust summaries provided the following purity/composition:

#### Crude Butadiene C4 Category

(1) CASRN 106-99-0, 1,3-Butadiene: In the robust summaries, the purity of 1,3-butadiene (supporting chemical for human health endpoints) is reported to be > 98.94%.

(2) CASRN 68476-52-8, C4 crude butadiene with low 1,3-butadiene content (stream containing ~10% 1,3-butadiene, 4% isobutene, 4% n-butane, 29% *trans*-2-butene, 29% 1-butene, 11%

isobutylene and 12% *cis*-2-butene). This stream is representative of CASRNs 25167-67-3, 64742-83-2, 68187-60-0, 68476-44-8, 68955-28-2 and 68954-7.

(3) CASRN 68955-28-2, Gases (petroleum) light steam-cracked, butadiene conc. (stream containing ~45% 1,3-butadiene, 20% butanes and 30% butenes)

(4) CASRN 68955-28-2, Gases (petroleum) light steam-cracked, butadiene conc. (stream containing ~67% 1,3-butadiene, 30% butanes, and 2% 1,2-butadiene)

### High Benzene Naphthas Category

(1) In CASRN71-43-2, Benzene: In the robust summaries, the purity of benzene (supporting chemical for human health endpoints) is reported to be > 99%.

(2) Dripolene, Pyrolysis Gasoline (stream, CASRN not available)

(3) CASRN 68410-97-9, Hydrogenated pyrolysis gasoline (stream containing 55% benzene, 25% toluene, 10% xylene, 7% pentane, 7% ethyl benzene, 2% hexane, 3% cyclohexane)

(4) CASRN 64741-74-8, Rerun Tower Overheads (stream containing ~40% benzene, 13% toluene, 26% C5s, 20% other)—C5-10 Fraction of Pyrolysis Gasoline

The percent purity for supporting chemicals used in aquatic toxicity tests was as follows: ethylene (CASRN 74-85-1): >99.9%; pentane (CASRN 109-66-0): >95%; and 2-butene,2-methyl- (CASRN 513-35-9): >99%.

## 1.2 Physical-Chemical Properties

The physical-chemical properties of the sponsored substances contained in the pyrolysis C3+ and pyrolysis C4+ streams category and its supporting chemicals are summarized in Table 4. A description of the complex mixtures used for this category and the chemical structures of the specific compounds is provided in Appendix.

The components of this category are gasses that possess high vapor pressure and moderate water solubility.

**Table 4. Physical-Chemical Properties of Pyrolysis C3+ and Pyrolysis C4+ Streams and Supporting Chemicals<sup>1</sup>**

Property	SPONSORED CHEMICAL Pyrolysis C3+ and Pyrolysis C4+ Streams <sup>2</sup>	SUPPORTING CHEMICAL 1,3-Butadiene	SUPPORTING CHEMICAL Benzene
CASRN	64742-83-2; 68513-68-8	106-99-0	71-43-2
Molecular Weight	Complex mixture	54.09	70.14
Physical State	Gas	Gas	Liquid
Melting Point (°C)	-185.3 to -105.5 (measured) <sup>3</sup>	-108.9 (measured) <sup>3</sup>	5.5°C (measured) <sup>3</sup>
Boiling Point (°C)	-11.7 to 3.7 (measured) <sup>3</sup>	-4.4°C (measured) <sup>3</sup>	80°C (measured) <sup>3</sup>
Vapor Pressure (mm Hg at 25 °C)	1,600 to 2,610 (measured) <sup>3</sup>	2,110 (measured) <sup>3</sup>	94.8 mm Hg at 25°C (measured) <sup>3</sup>
Dissociation Constant (pK <sub>a</sub> )	Not applicable		
Henry's Law Constant (atm·m <sup>3</sup> /mol)	0.074 to 1.19 (measured) <sup>3</sup>	0.074 (measured) <sup>3</sup>	0.0055 atm·m <sup>3</sup> /mol (measured) <sup>3</sup>
Water Solubility (mg/L at 25°C)	48.8 to 735 (measured) <sup>3</sup>	735 (measured) <sup>3</sup>	1,790 mg/L at 25°C (measured) <sup>3</sup>
Log K <sub>ow</sub>	1.99 to 2.89 (measured) <sup>3</sup>	1.99 (measured) <sup>3</sup>	2.13 (measured) <sup>3</sup>

<sup>1</sup> Chemicals Manufacturing Association Olefins Panel, HPV Implementation Task Group. May 5, 2004. Revised Test Plan and Robust Summary for the Crude Butadiene C4 Category. Available online from: <http://www.epa.gov/chemrtk/pubs/summaries/olefins/c12064tc.htm> as of August 18, 2010.

<sup>2</sup> Based on the chemical composition of this process stream (see Appendix A) data was derived from: propane, 2-methyl- (75-28-5); butane (106-97-8); 1-propene, 2-methyl- (115-11-7); 2-butene, (2Z)- (590-18-1); 2-butene, (2E)- (624-16-6); 1-butene (106-98-9); and 1,3-butadiene (106-99-0).

<sup>3</sup> SRC. The Physical Properties Database (PHYSPROP). SRC, Inc., Syracuse, NY. Available online from: <http://www.syrres.com/esc/physprop.htm> as of August 18, 2010.

## 2. General Information on Exposure

### 2.1 Production Volume and Exposure

The pyrolysis C3+ and pyrolysis C4+ streams category chemicals had an aggregated production and/or import volume in the United States greater than seven billion 760 million pounds in calendar year 2005.

- CASRN 64742-83-2: 1 billion pounds and greater;
- CASRN 68513-68-8: 100 to <500 million pounds;

CASRN 64742-83-2 and 68513-68-8: No industrial processing and uses and commercial and consumer uses were reported for these chemicals.

## 2.2 Environmental Exposure and Fate

The components of the pyrolysis C3+ and pyrolysis C4+ streams category are expected to possess high mobility in soil. 1,3-Butadiene and supporting chemical, 1-butene, were not readily biodegradable, achieving less than 5% biodegradation within 28 days in a closed bottle test (OECD 301D); however, several substances in this category have been shown to degrade using mixed microbial or pure cultures isolated from various sources. Propane, 2-methyl- achieved 49% mineralization in 20 days following a 6 day lag period and using the mixed microbial cultures isolated from municipal sewage sludge. Butane was completely degraded after 34 days using the same set of cultures. The half-life of 1,3-butadiene in aerobic waters has been reported as approximately 7 days and the half-life in anaerobic waters was reported as 28 days. Volatilization of these substances is expected to be high based on the Henry's Law constants of these substances. The rate of hydrolysis is expected to be negligible since the substances in this category do not possess functional groups that hydrolyze under environmental conditions. The members of the pyrolysis C3+ and pyrolysis C4+ streams category are expected to possess low persistence (P1) and low bioaccumulation potential (B1).

The environmental fate properties are provided in Tables 5.

<b>Table 5. Environmental Fate Characteristics of Pyrolysis C3+ and Pyrolysis C4+ streams<sup>1</sup> and Supporting Chemicals</b>			
<b>Property</b>	<b>SPONSORED CHEMICAL Pyrolysis C3+ and Pyrolysis C4+ streams<sup>2</sup></b>	<b>SUPPORTING CHEMICAL 1,3-Butadiene</b>	<b>SUPPORTING CHEMICAL Benzene</b>
CASRN	64742-83-2; 68513-68-8	106-99-0	71-43-2
Photodegradation Half-life	1.9–52.6 hours (estimated) <sup>3</sup>	1.9 hours (estimated) <sup>3</sup>	5.14 days (estimated) <sup>4</sup>
Hydrolysis Half-life	Stable		
Biodegradation	No data	0–4% after 28 days (not readily biodegradable) <sup>4</sup> ; Half-life 7 days in aerobic water and 28 days in anaerobic waters <sup>5</sup>	40% in 14 days (readily biodegradable) <sup>5</sup>
Bioaccumulation Factor	BAF = 10–61 (estimated) <sup>3</sup>	BAF = 10 (estimated) <sup>4</sup>	BAF = 15 (estimated) <sup>4</sup>
Log K <sub>oc</sub>	1.5–1.6 (estimated) <sup>3</sup>	1.6 (estimated) <sup>4</sup>	2.16 (estimated) <sup>4</sup>
Fugacity (Level III Model) <sup>4</sup>			
Air (%)	3.0–48.4	5.7	31.4
Water (%)	50.6–94.6	90.9	41.3
Soil (%)	0.7–3.0	3.0	26.8
Sediment (%)	0.2–0.3	0.3	0.372
Persistence <sup>6</sup>	P1 (low)	P1 (low)	P1 (low)
Bioaccumulation <sup>6</sup>	B1 (low)	B1 (low)	B1 (low)

<sup>1</sup>Chemicals Manufacturing Association Olefins Panel, HPV Implementation Task Group. May 5, 2004. Revised Test Plan and Robust Summary for the Crude Butadiene C4 Category. Available online from:

<http://www.epa.gov/chemrtk/pubs/summaries/olefins/c12064tc.htm> as of August 18, 2010.

<sup>2</sup>Based on the chemical composition of this process stream (see Appendix A) data was derived from: propane, 2-methyl- (75-28-5); butane (106-97-8); 1-propene, 2-methyl- (115-11-7); 2-butene, (2Z)- (590-18-1); 2-butene, (2E)- (624-16-6); 1-butene (106-98-9); and 1,3-butadiene (106-99-0).

<sup>3</sup>U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: <http://www.epa.gov/opptintr/exposure/pubs/episuite.dll> as of August 18, 2010.

<sup>4</sup>National Institute of Technology and Evaluation. 2002. Biodegradation and Bioaccumulation of the Existing Chemical Substances under the Chemical Substances Control Law. Available online from:

[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 August 18, 2010.

<sup>5</sup>Capel P., Larson S. 1995. A chemodynamic approach for estimating losses of target organic chemicals from water during sample holding time. *Chemosphere* 30: 1097–1107.

<sup>6</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:** The pyrolysis C3+ and pyrolysis C4+ streams category consists of two process streams (The pyrolysis C3+ stream and pyrolysis C4+ streams) which arise from the production processes associated with ethylene manufacturing. The substances of this category are gasses possessing high vapor pressure and moderate water solubility. All category members are expected to possess high mobility in soil. Volatilization is expected to be high. The rate of hydrolysis is expected to be negligible. The rate of atmospheric photooxidation is expected to be slow to rapid for the members of this category. The members of the pyrolysis C3+ and pyrolysis C4+ streams category are expected to possess 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 6. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

#### *Acute Oral Toxicity*

##### ***Benzene (CASRN 71-43-2, supporting chemical)***

See human health data at: [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf)

**Rat LD<sub>50</sub> > 810-10,000 mg/kg**

##### ***Dripolene (No CASRN, pyrolysis gasoline, supporting chemical)***

Sprague-Dawley rats (5/sex/dose) were administered dripolene via gavage at 2000 mg/kg-bw and observed for 14 days. No mortalities were observed.

**LD<sub>50</sub> > 2000 mg/kg**

##### ***Hydrogenated pyrolysis gasoline (CASRN 68410-97-9 containing 55% benzene, supporting chemical)***

Fischer 344 rats (5/sex/dose) were administered hydrogenated pyrolysis gasoline via oral route at 4200, 4600, 5000 and 5400 mg/kg-bw and observed for 14 days. Mortalities were observed at 5000 and 5400 mg/kg-bw.

**LD<sub>50</sub> = 5170 mg/kg**

##### ***Rerun Tower Overheads, pyrolysis gasoline (CASRN 64741-74-8, containing 40% benzene, supporting chemical)***

Sprague-Dawley rats (5/sex/dose) were administered rerun tower overheads (~40% benzene, 13% toluene, 26% C5s, 20% other) via gavage at 2000 mg/kg-bw and observed for 14 days. No mortalities were observed.

**LD<sub>50</sub> > 2000 mg/kg**

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

#### ***Gases (petroleum) light steam-cracked, butadiene conc. (CASRN 68955-28-2 containing ~45% 1,3-butadiene, supporting chemical)***

Fischer 344 rats (5/sex/dose) were exposed via whole body inhalation to CASRN 68955-28-2 (approximately 45% 1,3-butadiene, 20% butanes and 30% butenes) at 5300 mg/m<sup>3</sup> (2331 ppm) for 4 hours and observed for 14 days. No mortalities were observed.

**LC<sub>50</sub> > 5.3 mg/L**

#### ***1,3-Butadiene (CASRN 106-99-0, >99% purity, supporting chemical)***

(1) In the rat, 4-hour LC<sub>50</sub> value was reported to be 285 mg/L (129,000 ppm). Information is not available on the strain, age, number and sex, number of exposure concentrations or post observation period.

**LC<sub>50</sub> = 129,000 ppm**

(2) See human health data at [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/butadienereport019.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/butadienereport019.pdf).

#### ***Hydrogenated Pyrolysis Gasoline (CASRN 68410-97-9 containing 55% benzene, supporting chemical)***

Fischer 344 rats (5/sex/concentration) were exposed to CASRN 68410-97-9 via whole body inhalation at 12,408 ppm for 4 hours and observed for 14 days. No mortalities occurred.

**LC<sub>50</sub> > 12,408 ppm**

#### ***Benzene (CASRN 71-43-2, supporting chemical)***

(1) Sprague-Dawley rats (10 females/test concentration) were exposed to benzene via inhalation at unspecified concentrations for 4 hours and observed for 14 days following dosing. Mortality was not specified.

**LC<sub>50</sub> = 43.7 mg/L**

(2) See human health data at [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf)

### ***Acute Dermal Toxicity***

#### ***Dripolene (No CASRN, pyrolysis gasoline, supporting chemical)***

New Zealand White rabbits (3/sex/dose) were administered dripolene via the dermal route at 2000 mg/kg-bw for 24 hours and observed for 14 days. No mortalities were observed.

**LD<sub>50</sub> > 2000 mg/kg**

***Rerun Tower Overheads, pyrolysis gasoline (, CASRN 64741-74-8, containing 40% benzene, supporting chemical)***

New Zealand White rabbits (3/sex/dose) were administered rerun tower overheads (~40% benzene, 13% toluene, 26% C5s, 20% other) via the dermal route at 2000 mg/kg-bw for 24 hours and observed for 14 days. No mortalities were observed.

**LD<sub>50</sub> > 2000 mg/kg**

***Repeated-Dose Toxicity***

***Gases (petroleum) light steam-cracked, butadiene conc. (CASRN 68955-28-2, ~45% 1,3-butadiene, supporting chemical)***

Fischer 344 rats (5/sex/dose) were exposed to CASRN 68955-28-2 gas (~45% 1,3-butadiene, 20% butanes and 30% butenes) via whole-body inhalation at concentrations of 0, 1110 and 11,140 ppm, for 6 hours/day for 9 days. Most rats in both exposure groups appeared normal throughout the study. Nasal discharge was observed in some rats of both groups and at a greater incidence in the high-exposure group. There were no differences between the control and exposed groups for mean body weight, organ weight, hematology or blood chemistry values. There were no exposure-related histopathologic changes in any of the organs or tissues examined.

**NOAEC = 11,140 ppm/day** (highest concentration tested)

***C4 crude butadiene (CASRN 68476-52-8, ~10% 1,3-butadiene content, supporting chemical)***

In a combined repeated-dose/reproductive/developmental toxicity screening test, Sprague-Dawley rats (12/sex/concentration) were exposed to CASRN 68476-52-8 vapor (~10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% *trans*-2-butene, 29% 1-butene, 11% isobutylene and 12% *cis*-2-butene) via whole-body inhalation, at concentrations of 0, 2, 10 or 20 mg/L for 6 hours/day, 7 days/week for 36 – 37 days. (Targeted exposure concentrations were not met on one entire exposure duration and during brief periods on a few other days. However, the affected instances were limited relative to the total duration of the study and did not have significant impact on study integrity.) There were no deaths and no treatment-related clinical signs were noted. No differences in body weights and food consumption were observed for the males or females at any concentration throughout the duration of the study. Sensory evaluation, rectal temperature, fore/hindlimb grip performance and motor activity data revealed no treatment-related effects. No treatment-related changes were noted for prothrombin time, hematology values or clinical chemistry measurements in males and females at any concentration. There were no effects on organ weights, gross pathology or histopathology in any of the exposed groups when compared to their respective controls.

**NOAEC = 20 mg/L/day** (highest concentration tested)

***1,3-Butadiene (CASRN 106-99-0, >99% purity, supporting chemical)***

(1) Sprague-Dawley rats (40/sex/concentration) were exposed to 1,3-butadiene gas (purity >99.2%, containing 120 ppm t-butyl catechol;) via whole-body inhalation at concentrations of 0, 1000, 2000, 4000 or 8000 ppm for 6 hours/day, 5 days/week for 13 weeks. Interim sacrifices were performed on 10 rats/sex/group after 2 and 6 weeks of exposure. Increased salivation was observed in females after 8 weeks and decreased grooming (stained fur) in the males after 10 weeks. No other exposure-related clinical signs were observed. Male rats showed slight reductions in body weight gains compared to the controls. Food consumption, blood and urine analyses, measurement of brain cholinesterase activity, organ weight measurements and histopathological examinations (high dose only) were comparable to control values.

**NOAEC = 8000 ppm/day** (highest concentration tested)

(2) In an NTP study, B6C3F1 mice (10/sex/dose) were exposed to 1,3-butadiene gas (rubber grade, containing 0.02% t-butyl catechol;) via whole-body inhalation at concentrations of 0, 625, 1250, 2500, 5000 or 8000 ppm for 6 hours/day, 5 days/week for 14 weeks (64 exposures). Because four male mice in the high-exposure group died by day 4, another two groups of 10 male mice each were restarted (control and 8000 ppm). At the end of the 95- or 93-day (restart) studies, surviving mice were sacrificed. Histopathologic examination was conducted on animals from the control and high-dose groups. Mortalities and/or morbidities occurred at 1250 ppm and above. Body weights were decreased at 2500 ppm and above in males and at 5000 ppm and above in females. No exposure-related histopathological changes were observed.

[This study was conducted at IBT.]

**LOAEC = 1250 ppm/day** (based on mortalities)

**NOAEC = 625 ppm/day**

(3) In an NTP carcinogenicity study, B6C3F1 mice (50/sex/concentration) were exposed to 1,3-butadiene gas via whole-body inhalation at concentrations of 0, 625 or 1250 ppm, 6 hours/day, 5 days/week for 60 – 61 weeks. Survival was markedly reduced in exposed animals due primarily to the development of malignant tumors. Histopathological examination was conducted. A wide range of organs was affected by exposure to butadiene (see also under carcinogenicity). Non-neoplastic changes at 625 and 1250 ppm included ovarian and testicular atrophy, congestion, hemorrhage and hyperplasia of the lungs, hemorrhage and necrosis of the liver, thymus and bone marrow atrophy, epithelial hyperplasia of the forestomach and endothelial hyperplasia and mineralization of the heart. Chronic inflammation and fibrosis developed in the nasal cavities of males exposed to 1250 ppm. 1,3-Butadiene caused severe toxicity in mice at these concentrations. ([http://ntp-apps.niehs.nih.gov/ntp\\_tox/index.cfm?fuseaction=ntpsearch.searchhome](http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchhome))

***Benzene (CASRN 71-43-2, supporting chemical)***

(1) In a 10-week study, CD-1 mice (11 – 12 males/test concentration) were exposed to benzene vapor via inhalation at 0 or 9.6 ppm (0 or 0.03 mg/L), 6 hours/day, 5 days/week. Hematological parameters were evaluated at the end of exposure. No mortality was observed. Increases were observed in spleen weight, total nucleated cells per spleen and nucleated red blood cells (RBCs) at 0.03 mg/L.

**LOAEC ~ 0.03 mg/L/day** (based on increases in spleen weight, total nucleated cells per spleen and nucleated RBCs)

**NOAEC = Not established**

(2) In a 13-week study, CD-1 mice (40/sex/test concentration) were exposed via whole-body inhalation to benzene as a vapor at 0, 1, 10, 30 or 300 ppm (approximately 0, 0.003, 0.03, 0.10 or 0.96 mg/L), 6 hours/day, 5 days/week. Endpoints included behavior, body weights, organ weights, clinical pathology, gross pathology, histopathology, hematology and clinical chemistry. At ~0.96 mg/L, hematological effects included decreases in RBC counts, WBC counts, platelets, hemoglobin, myeloid/erythroid ratios and hematocrit. Other effects at ~0.96 mg/L included femoral myeloid hypoplasia, extramedullary hemotopoiesis in the spleen, thymic atrophy, decreases in absolute and relative testis weights, minimal to moderately severe bilateral atrophy/degeneration of testes, moderate to moderately severe decreases in spermatozoa and a minimal to moderate increase in abnormal sperm morphology. Bilateral ovarian cysts were observed in four females at 0.96 mg/L. Histopathological changes were also observed in mesenteric and mandibular lymph nodes, as well as in the liver at ~0.96 mg/L.

**LOAEC ~ 0.96 mg/L/day** (based on effects hematopoietic system, spleen, thymus, testes, ovaries, liver and lymphnodes)

**NOAEC ~ 0.10 mg/L/day**

(3) Several studies are described in the OECD SIDS documents at:

[http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf).

***Reproductive Toxicity***

***C4 crude butadiene (CASRN 68476-52-8, ~10% 1,3-butadiene content, supporting chemical)***

In the combined repeated-dose/reproductive/developmental toxicity screening test in rats described above, the study design included a main study for repeated-dose toxicity endpoints and a reproductive/developmental toxicity satellite groups (12 females/dose) that were exposed to CASRN 68476-52-8 vapor via inhalation at concentrations of 0, 2, 10 or 20 mg/L, for 6 hours/day, 7 days/week for 2 weeks prior to mating, during mating (up to 2 weeks) and continuing through day 19 of gestation. (Males from the main study were used to breed these females.) Males (from the main study) were exposed for 36 – 37 days. The dams were allowed to deliver their litters, which were retained until postnatal day 4. There were no deaths and no treatment-related clinical observations were noted. No differences in parental body weights, body weight gains or feed consumption were observed at any dose level throughout the duration of the study. There were no treatment-related effects on any reproductive parameters including measures of reproductive performance (mating, conception and fertility, time to mating,

gestation length, and litter size) or offspring survival (gestation and postnatal survival indices, percent pre- and post-implantation loss).

**NOAEC (systemic/reproductive toxicity) = 20 mg/L/day** (highest concentration tested)

***1,3-Butadiene (CASRN 106-99-0, supporting chemical)***

(1) A recent (2002) Integrated Risk Information System (IRIS) review by EPA on 1,3-butadiene is available at <http://www.epa.gov/ncea/iris/subst/0139.htm>.

The most sensitive reproductive endpoint observed in subchronic studies with CASRN 106-99-0 was fetal deaths in dominant lethal studies in mice exposed for 28-days at 65 ppm (see *Other* section for details); the NOAEC was 12.5 ppm. In two-year bioassays, the most sensitive reproductive effects were ovarian atrophy in female mice at 6.25 ppm and testicular atrophy in male mice at 625 ppm. The NOAEC for reproductive toxicity in female mice was not established and in male mice was 200 ppm (see *Carcinogenicity* section for details).

(2) In a combined reproductive/developmental toxicity screening test (OECD TG 421), Sprague-Dawley rats (12/sex/concentration) were exposed whole-body to 1,3-butadiene as a vapor at 0, 300, 1500 or 6000 ppm (approximately 0, 0.66, 3.3 or 13.3 mg/L/day) for 6 hours/day. Animals of both sexes were exposed for 2 weeks prior to mating and 2 weeks during mating. Males continued to be exposed after mating for a total of 70 days. Females were exposed on gestation days 0 – 19 and postnatal days 5 – 18. After weaning on postnatal day 21, one male and one female from each litter were exposed for 7 days to the same concentration of 1,3-butadiene as its dam. Beginning on postnatal day 28, previously unexposed weanlings (1/sex/litter) were exposed for 7 days to the same concentration of 1,3-butadiene as their dams. Reproductive endpoints included assessments of gonadal function, mating behavior, conception, gestation and parturition (details not specified). Reductions in body weight parameters (details not specified) were observed in the parental generation and offspring at concentrations  $\geq 3.3$  mg/L. Transient reductions in food consumption were observed in the parental generation during the first week of exposure. Clinical signs at 13.3 mg/L/day included chromodacryorrhea, chromorhinorrhea and salivation in the parental generation and infrequent occurrences of dried red material in the perioral and perinasal regions of four exposed pups. No reproductive effects were observed. **NOAEC (reproductive toxicity) ~ 13.3 mg/L/day** (highest concentration tested)

(3) Male Sprague-Dawley rats (25/concentration) were exposed to 1,3-butadiene gas (purity >99.7%) via inhalation at concentrations of 0, 65, 400 or 1250 ppm 6 hours/day, 5 days/week for 10 weeks and then mated with untreated females. Pregnant females were sacrificed 20 days after the mating period ended. The uteri were examined for live/dead fetuses, early and late deaths and malformed fetuses. Mating frequency, period of coition, pregnancy rates and pre- or post-implantation loss were not affected by treatment. The number of implantation sites was reduced in the 65 ppm group, but the impact on reproductive toxicity was unclear as there were no post-implantation losses. All other parameters (early deaths, late deaths, including or excluding dead fetuses and fetal abnormalities) remained unchanged in all treatment groups. Study details are from TSCATS (OTS0001282).

**NOAEC (reproductive toxicity) = 1250 ppm/day** (highest concentration tested)

(4) See human health data at [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/butadienereport019.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/butadienereport019.pdf).

***Benzene (CASRN 71-43-2, supporting chemical)***

(1) In the 13-week inhalation study in CD-1 mice described previously, effects on male reproductive organs at 0.96 mg/L included decreases in absolute and relative testes weights, minimal to moderately severe bilateral atrophy/degeneration of testes, moderate to moderately severe decreases in spermatozoa and a minimal to moderate increase in abnormal sperm morphology. In addition, bilateral ovarian cysts were observed in four females at 0.96 mg/L.

(2) See human health data at: [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf).

***Developmental Toxicity***

***C4 crude butadiene (CASRN 68476-52-8, ~10% 1,3-butadiene content, supporting chemical)***

In the combined repeated-dose/reproductive/developmental toxicity screening test in Sprague-Dawley rats described above, additional reproductive/developmental toxicity satellite groups (12 females/dose) were exposed to the C4 crude butadiene vapor (~10% 1,3-butadiene, 4% isobutene, 4% n-butane, 29% *trans*-2-butene 29% 1-butene, 11% isobutylene and 12% *cis*-2-butene) via inhalation at concentrations of 0, 2, 10 or 20 mg/L, for 6 hours/day, 7 days/week for 2 weeks prior to mating, during mating (up to 2 weeks) and continuing through day 19 of gestation. The dams were allowed to deliver their litters, which were retained until postnatal day 4. There were no deaths or treatment-related clinical observations noted. No differences in parental body weights, body weight gains or feed consumption were observed at any dose level tested throughout the duration of the study. There were no treatment-related effects on any developmental parameters including offspring survival, gestation and postnatal survival indices, percent pre- and post-implantation loss or grossly visible abnormalities. **NOAEC (maternal/developmental toxicity) = 20 mg/L/day** (highest concentration tested)

***1,3-Butadiene (CASRN 106-99-0, >99% purity, supporting chemical)***

(1) CD-1 Swiss mice (18 – 22 pregnant females/concentration) were exposed to 1,3-butadiene gas (purity 99.88%) via inhalation at concentrations of 0, 40, 200 or 1000 ppm for 6 hours/day on days 6 – 15 of gestation. There were decreases in maternal body weight gains at 200 (14%) and 1000 ppm (20%). Fetal weights were reduced in both males and females at 200 (16% less than control and 1000 ppm (22% less than control) ; placenta weights were reduced for corresponding male fetuses at 200 ppm and both males and females at 1000 ppm. There were no significant differences in percent resorptions or malformations per litter, although there was an increase in fetal variations (supernumary ribs and reduced ossification of sternbrae) at the two highest concentrations. A slight but statistically significant decrease in male fetal weight (95% of control) was seen at 40 ppm.

**LOAEC (maternal and developmental toxicity) = 200 ppm/day** (based on decreased maternal body weight gains, decreased fetal and placental weights and increased incidence of fetal variations)

**NOAEC (maternal and developmental toxicity) = 40 ppm/day**

(2) In an NTP study, Sprague-Dawley rats (24 – 28 pregnant females/dose) were exposed to 1,3-butadiene gas (purity 99.88%) via inhalation at doses of 0, 40, 200 or 1000 ppm 6 hours/day on days 6 – 15 of gestation. The only effect observed was decreased body weight gains in the dams at 1000 ppm. The percentage of pregnant animals and number of litters with live fetuses were unaffected by treatment. There were no differences among the groups for number of live fetuses per litter, percent resorptions or malformations per litter, placental or fetal body weights or sex ratio. There was no evidence of developmental toxicity or adverse reproductive effects in any of the exposed groups.

**LOAEC (maternal toxicity) = 1000 ppm/day** (based on decreased maternal body weight gains)

**NOAEC (maternal toxicity) = 200 ppm/day**

**NOAEC (developmental toxicity) = 1000 ppm/day** (highest concentration tested)

(3) Pregnant Sprague-Dawley rats (40 in control group, 24/concentration in treatment groups and 26 in a positive control group) were exposed to 1,3-butadiene gas via inhalation at concentrations of 0, 200, 1000 or 8000 ppm for 6 hours/day from day 6 to 15 of gestation and sacrificed on day 20. No treatment-related mortalities or clinical signs were observed. There was a dose-related decrease in maternal body weights and body weight gains at all concentrations. There was no effect on pregnancy rate, implantation or pre-implantation loss or gravid uterus weight. Post-implantation loss was slightly higher (but not statistically significant) at all concentrations than in the control group. Mean fetal weight and crown/rump length were lower than the control group at all concentrations; statistically significant at 8000 ppm. Fetal sex ratio was unaffected. There was a higher incidence of minor fetal defects and variants, a decrease in fetal growth rates at all dose levels and an increase in the incidence of major fetal defects (wavy ribs) at 8000 ppm. Overall, there was dose-related embryonic growth retardation at all concentrations. Study details are from TSCATS (OTS0505459).

**LOAEC (maternal/developmental toxicity) = 200 ppm/day** (based on decreased maternal body weight gains and fetal growth retardation, respectively)

**NOAEC (maternal/developmental toxicity) = Not established**

(1) In the combined inhalation reproductive/developmental toxicity screening test in Sprague-Dawley rats described previously, developmental endpoints included assessments of conception, parturition, lactation and development of offspring (details not specified). No developmental effects were observed.

**LOAEC (maternal toxicity) = 3.3 mg/L** (based on reductions in body weight parameters)

**NOAEC (maternal toxicity) = 0.66 mg/L**

**NOAEC (developmental toxicity) = 13.3 mg/L** (highest concentration tested)

(5) See human health data at [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/butadienereport019.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/butadienereport019.pdf).

***Rerun Tower Overheads, pyrolysis gasoline (CASRN 64741-74-8, containing 40% benzene, supporting chemical)***

New Zealand White rabbits (16 females/group) were administered rerun tower overheads (~40% benzene, 13% toluene, 26% C5s, 20% other) via gavage at 0, 10, 25 or 50 mg/kg-day during days 6 through 28 of gestation. There were no treatment-related changes at any dose level for maternal survival, body weight, number of corpora lutea, total implantations, fetal sex

index fetal body weight or number of litters with malformations. Two control dams and one 50 mg/kg-day dam had resorptions. Treatment-related effects on maternal toxicity included a slight increase in matted haircoat and a slight reduction in fecal material beneath cages in rabbits at 50 mg/kg-day. Maternal survival was 100% in all groups.

**LOAEL (maternal toxicity) = 50 mg/kg-day** (based on one abortion)

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

**NOAEL (developmental toxicity) = 50 mg/kg-day** (highest dose tested)

***Benzene (CASRN 71-43-2, supporting chemical)***

(1) Pregnant Swiss-Webster Crl:CFW(SW)Br mice (15/dose) were exposed to benzene as a vapor at 0, 5, 10 or 20 ppm (approximately 0, 0.016, 0.032 or 0.064 mg/L), 6 hours/day on gestation days 6 – 15. Mice (5/dose) were sacrificed on gestation day 16. Endpoints included the numbers of live, dead and resorbed fetuses, fetal weights and external gross morphological malformations, RBC and WBC counts and hemoglobin analysis of fetal blood and numbers of cells in the hematopoietic differentiating proliferating pool (DPP) of fetal livers. Additional mice (5/dose) were allowed to proceed through normal parturition and on day 2 postpartum, pups were subjected to hematological examination, as above. The remaining mice (5/dose) were allowed to proceed through normal parturition and after 6 weeks postpartum, peripheral blood samples were removed from offspring for RBC and WBC counts; additionally, cells of the DPP were enumerated in the spleen and femoral bone marrow. No mortality, morbidity or weight loss of dams was observed during the exposure. No effects of exposure were observed on litter sizes, sex ratios, pup weights and numbers of dead, resorbed or malformed fetuses. Reduced counts of erythroid precursor cells (early nucleated cells) were observed in the peripheral blood of 2-day old pups exposed to benzene (concentrations not specified). Depressed numbers of late nucleated red cells and elevated numbers of granulocytic precursor cells (non-dividing granulocytes) were observed in the peripheral blood of 2-day old pups exposed to 0.064 mg/L. Lower numbers of early and late nucleated RBCs were observed in the livers of 2-day old pups at 0.064 mg/L. Elevated numbers of blasts, dividing/non-dividing granulocytes and lymphocytes were observed in the livers of 2-day old pups and spleens and femurs of 6-week old offspring of dams exposed to 0.064 mg/L.

**NOAEC (maternal toxicity) ~ 0.064 mg/L/day** (highest concentration tested)

**LOAEC (developmental toxicity) ~ 0.064 mg/L/day** (based on effects on the hematopoietic system)

**NOAEC (developmental toxicity) ~ 0.032 mg/L/day**

(2) In a modified prenatal developmental toxicity study, female Sprague-Dawley rats (26 /dose) were exposed to benzene as a vapor at 0, 1, 30 or 300 ppm (approximately 0, 0.0032, 0.096 or 0.96 mg/L), 6 hours/day, 5 days/week for a 10-week pre-mating and mating period and daily on gestation days 0 – 20 and lactation days 5 – 20. Endpoints included maternal body weight, pregnancy rate, length of gestation, numbers of live and dead pups, sex ratio, pup survival, pup body weight change and pup organ weights. Reduced body and liver weights were observed in female pups at 0.96 mg/L. [EPA's Toxicological Review of Benzene, 2002 (EPA/635/R-02/001F)].

**NOAEC (maternal toxicity) ~ 0.96 mg/L/day** (highest concentration tested)

**LOAEC (developmental toxicity) ~ 0.96 mg/L/day** (based on reduced body and liver weights in female pups)

**NOAEC (developmental toxicity) ~ 0.096 mg/L/day**

(3) See human health data at: [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf).

***Genetic Toxicity – Gene Mutation***

***In vitro***

***Crude Butadiene C4 Category***

***1,3-Butadiene (CASRN 106-99-0, >99% purity, supporting chemical)***

(1) *Salmonella* strains TA97, TA98, TA100, TA1535 were exposed to 1,3-Butadiene at concentrations of 0, 30, 40, 50 and 60% in air, with and without rat, mouse or human liver S9 metabolic activation systems. Both positive and negative controls were run and they responded appropriately. 1,3-Butadiene induced revertants only in strain TA1535. At 30%, slightly higher activity was noted using the mouse liver S9 activation system than the rat or human S9 activation system. At concentrations > 30%, the number of revertants decreased in the presence of rat or human S9. Results from the human S9-activated treatments did not differ substantially from those of the non-activated treatment. The results were similar for rat liver S9 activation system and uninduced mouse liver S9 activation system. Increasing the concentration of rat S9 (from 0.8 to 4.0 mg/plate) had no effect on the number of revertants. Positive control responded appropriately. Cytotoxic concentration was not reported.

**1,3-Butadiene was mutagenic in this assay.**

(2) See human health data at [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/butadienereport019.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/butadienereport019.pdf)

***Gases (petroleum) light steam-cracked, butadiene conc. (CASRN 68955-28-2 containing ~67% 1,3-butadiene, supporting chemical)***

(1) *Salmonella* strains TA98, TA100, TA1535, TA1537, TA1538 were exposed to gases (petroleum) light steam-cracked, butadiene conc. (~67% 1,3-butadiene, 30% butanes and 2% 1,2-butadiene) with and without metabolic activation at concentrations of 25, 50, 75 or 100 µL/plate. Both positive and negative controls were run; however, their responses were not reported. Cytotoxicity was noted at > 75 µL in TA 100 and > 100 µL in TA1537 in the preliminary assay. Some inconsistencies in toxicity with increasing dose level were noted that were attributed to the volatility of the test substance. None of the five strains exhibited reversion frequencies substantially different from controls.

**Gases (petroleum) light steam-cracked, butadiene conc. was not mutagenic in this assay.**

(2) Mouse lymphoma cells ((L5178Y) were exposed to gases (petroleum) light steam-cracked, butadiene conc. (~67% 1,3-butadiene, 30% butanes and 2% 1,2-butadiene) at concentrations of 10, 12.5, 15, 17.5, 20, 22.5, 25, 27.5, 30, 35, 40 or 45 µL/mL without metabolic activation and 2.5, 5, 7.5, 10, 12.5, 15, 17.5, 20, 22.5 or 25 µL/mL with metabolic activation. Both positive and negative controls were run. Positive control responses were not reported. Without metabolic activation, mutant frequencies and total number of mutants were increased at 20.0 and

22.5 µL/mL. Cytotoxic concentration was not reported. There were no differences in mutant frequency for the S9 activated cultures.

**Gases (petroleum) light steam-cracked, butadiene conc. was mutagenic in the absence of metabolic activation in this assay.**

***Hydrogenated Pyrolysis Gasoline (CASRN 68410-97-9 containing 55% benzene, supporting chemical)***

*Salmonella typhimurium* strains TA1535, TA1537, TA98 and TA100 and *Escherichia coli* strain WP2(uvrA) were exposed to hydrogenated pyrolysis gasoline (55% benzene, 25% toluene, 10% xylene, 7% pentane, 7% ethyl benzene, 2% hexane, 3% cyclohexane) at 0, 33, 100, 333, 1000, 3333 or 10,000 µg/plate with and without metabolic activation. Cytotoxicity was not observed in any bacterial strain. Positive and negative controls were included and responded appropriately.

**Hydrogenated pyrolysis gasoline was not mutagenic in this assay.**

***Rerun Tower Overheads, pyrolysis gasoline (CASRN 64741-74-8, containing 40% benzene, supporting chemical)***

(1) *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to rerun tower overheads (~40% benzene, 13% toluene, 26% C5s, 20% other) at concentrations ranging from 0 to 3.1 µL/-plate with and without metabolic activation. Cytotoxicity was observed at 0.97 µL/plate without metabolic activation and at 3.1 µL/plate with metabolic activation. Positive and negative controls were included. The positive control responded appropriately.

**Rerun tower overheads was not mutagenic in this assay.**

(2) Mouse lymphoma L5178Y TK+/- cells were exposed to rerun tower overheads at doses ranging from 0 to 0.36 µL/mL with and without metabolic activation. Positive and negative controls were included. The positive control responded appropriately. Rerun tower overheads induced an increase in mutant frequency of mouse lymphoma cells without metabolic activation at the two highest concentrations tested (0.10 and 0.75 µL/mL), but was not mutagenic in this presence of S9 activation.

**Rerun tower overheads was mutagenic in this assay.**

***Benzene (CASRN 71-43-2, supporting chemical)***

(1) *Salmonella typhimurium* strains TA98, TA100, TA104 and TA1535 were exposed to benzene as a vapor at concentrations of 0, 3, 6, 15, 30, 100, 300 or 1000 ppm with and without metabolic activation. A positive control was not used. Exposure to benzene increased the mutation frequency in TA100, TA104 and TA1535 with activation. Cytotoxicity was not specified.

**Benzene was mutagenic in this assay.**

(2) See human health data at: [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf).

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

### ***In vivo***

#### ***C4 crude butadiene (CASRN 68476-52-8, ~10% 1,3-butadiene content, supporting chemical)***

In a mammalian erythrocyte micronucleus assay, B6C3F1 mice (6/sex/dose) were exposed to C4 crude butadiene (low 1,3-butadiene content; approximately 10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% *trans*-2-butene, 29% 1-butene, 11% isobutylene and 12% *cis*-2-butene) at concentrations of 0, 0.5, 10 and 20 mg/L via whole-body inhalation for 4 hours/day for 2 days. Twenty four hours after the second treatment, bone marrow was collected and smears were prepared. Statistically significant increases in the frequencies of micronucleated polychromatic erythrocytes were seen (MN-PCE) in both sexes of all treated groups compared to the negative controls. The positive control responded appropriately.

**C4 crude butadiene (low 1,3-butadiene content) induced chromosomal aberrations in this assay.**

#### ***Gases (petroleum) light steam-cracked, butadiene conc. (CASRN 68955-28-2 containing ~45% 1,3-butadiene, supporting chemical)***

In a mammalian erythrocyte micronucleus assay, Crl:CD-1 BR Swiss mice (10/sex/dose) were exposed to gases (petroleum) light steam-cracked, butadiene conc. (~ 45% 1,3-butadiene, 20% butanes and 30% butenes) at concentrations of 10,780, 20,671 or 35,430 ppm via whole-body inhalation for 2 hours/day for 2 days. Following the exposure, five mice/sex/group were sacrificed on days 3 and 4 and bone marrow smears were prepared. Positive control animals (5/sex) were sacrificed on day 3 only. No mice died during the study; the only clinical observation was an apparent unconsciousness during exposure. There were no body weight differences. Mice in the exposed groups showed increased micronuclei formation at all levels in both sexes. There was no change in the polychromatic/normochromatic erythrocytes (PCE/NCE) ratio in any group. The negative and positive control groups produced appropriate responses.

**Gases (petroleum) light steam-cracked, butadiene conc. induced chromosomal aberrations in this assay.**

#### ***1,3-Butadiene (CASRN 106-99-0 > 99% purity, supporting chemical)***

(1) In a mammalian erythrocyte micronucleus assay, Wistar rats (10 males/dose) and CB6F1 mice (20 females/dose) were exposed to 1,3-butadiene at concentrations of 0, 50, 200 or 500 ppm via inhalation for 6 hours/day for 5 days. An additional group of mice was exposed to 1300 ppm. The animals were sacrificed 1 day after the last exposure and smears of peripheral blood and bone marrow erythrocytes were prepared. In rats no effects on micronuclei frequency were seen in the peripheral blood or bone marrow at all exposure concentrations. In mice, 1,3-butadiene induced micronuclei in peripheral blood and bone marrow erythrocytes at  $\geq 50$  ppm.

**1,3-Butadiene induced chromosomal aberrations in mouse erythrocytes in this assay.**

(2) In a mammalian erythrocyte micronucleus assay, Syrian hamsters (20 males) and B6C3F1 mice (20 males) were exposed to 1,3-butadiene via whole-body inhalation at concentrations of

0 (room air) or 1000 ppm, 6 hours/day for 2 consecutive days. Twenty four hours after the final exposure animals were euthanized and bone marrow slides were prepared and evaluated for micronuclei. In mice and hamsters a statistically significant ( $p < 0.01$ ) increase in micronuclei was seen compared to controls. 1,3-Butadiene was active in inducing micronuclei in bone marrow erythrocytes. Study details are from TSCATS (OTS0524007).

**1,3-Butadiene induced chromosomal aberrations in this assay.**

(3) 1,3-Butadiene (> 500 ppm) was tested in male mice to assess chromosomal damage in immature male germ cells for 6 hours/day for 5 days. The mean frequency of micronucleated cells was enhanced at all exposure levels. Study details are from TSCATS (OTS0556235).

**1,3-Butadiene induced chromosomal aberrations in this assay.**

(4) See human health data at [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/butadienereport019.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/butadienereport019.pdf).

***Hydrogenated Pyrolysis Gasoline (CASRN 68410-97-9 containing 55% benzene, supporting chemical)***

In a mammalian erythrocyte micronucleus assay, hydrogenated pyrolysis gasoline (55% benzene, 25% toluene, 10% xylene, 7% pentane, 7% ethyl benzene, 2% hexane, 3% cyclohexane) was tested in CRL:CD-1(ICR)BR Swiss mice (10/sex/dose) at concentrations of 0, 500, 1000 or 2000 mg/kg-bw administered via gavage once a day for 2 days. Another group of mice (15/sex) were administered hydrogenated pyrolysis gasoline at 2000 mg/kg-bw as a single dose. Negative and positive controls were included and responded appropriately. Hydrogenated pyrolysis gasoline did not induce micronucleated erythrocytes in the bone marrow of mice at any dose tested and did not induce cytogenetic damage.

**Hydrogenated pyrolysis gasoline did not induce chromosomal aberrations in this assay.**

***Benzene (CASRN 71-43-2, supporting chemical)***

(1) In a sister chromatid exchange assay, male Sprague-Dawley rats (5/dose) were exposed to benzene as a vapor at 0, 0.1, 0.3, 1, 3, 10 or 30 ppm for 6 hours. Upon sacrifice, lymphocytes were assayed for sister chromatid exchange. The use of a positive control was not specified. At doses  $\geq 3$  ppm, a dose-dependent increase in the frequency of sister chromatid exchange was observed.

**Benzene induced sister chromatid exchange in this assay.**

(2) In a micronucleus assay, male Sprague-Dawley rats (5/dose) were exposed to benzene as a vapor at 0, 0.1, 0.3, 1, 3, 10 or 30 ppm for 6 hours. The use of a positive control was not specified. Significant increases in the frequency of micronuclei were observed at doses  $\geq 1$  ppm.

**Benzene induced micronuclei in this assay.**

(3) In a sister chromatid exchange assay, male DBA/2 mice (5/dose) were exposed to benzene as a vapor at 0, 10, 100 or 1000 ppm for 6 hours; upon sacrifice, lymphocytes were assayed for sister chromatid exchange. The use of a positive control was not specified. Increases in the frequency of sister chromatid exchange were observed at all doses.

**Benzene induced sister chromatid exchange in this assay.**

(4) In a micronucleus assay, male DBA/2 mice (5/dose) were exposed to benzene as a vapor at 0, 10, 100 or 1000 ppm for 6 hours. The use of a positive control was not specified. Significant increases in the frequency of micronuclei were observed at all doses.

**Benzene induced micronuclei in this assay.**

### *Genetic Toxicity – Other*

#### *In vitro*

#### ***Gases (petroleum) light steam-cracked, butadiene conc. (CASRN 68955-28-2 containing ~45% 1,3-butadiene, supporting chemical)***

In an unscheduled DNA synthesis (UDS) assay, rat primary hepatocytes were exposed to gases (petroleum) light steam-cracked, butadiene conc. (~45% 1,3-butadiene, 20% butanes and 30% butenes) at concentrations of 0, 1000, 5000, 10,000 and 20,000 ppm. Cytotoxicity was seen at and above 10,000 ppm. A weak positive response was observed for UDS at 20,000 ppm (7.74 nuclear grain counts vs. 1.24 in the air control vs. 107.13 in the positive control). A slight increase in UDS was also noted at 1000, 5000 and 10,000 ppm (4.29 – 5.14) compared to the air control. Both positive and negative controls were run and responded appropriately.

**Gases (petroleum) light steam-cracked, butadiene conc. induced unscheduled DNA synthesis in this assay.**

#### ***Hydrogenated Pyrolysis Gasoline (CASRN 68410-97-9 containing 55% benzene, supporting chemical)***

In an unscheduled DNA synthesis assay, hydrogenated pyrolysis gasoline (55% benzene, 25% toluene, 10% xylene, 7% pentane, 7% ethyl benzene, 2% hexane, 3% cyclohexane) was tested on primary hepatocytes derived from Fischer 344 male rats at concentrations of 8, 16, 32, 64, 128, 256, 512 or 1024 µg/mL. Cytotoxicity was seen at concentrations of 512 and 1024 µg/mL. Positive and negative controls were included and responded appropriately. Unscheduled DNA synthesis was not observed at any dose level with sufficient cells to be analyzed.

**Hydrogenated pyrolysis gasoline did not induce unscheduled DNA synthesis in this assay.**

#### ***Rerun Tower Overheads, pyrolysis gasoline ( CASRN 64741-74-8, containing 40% benzene, supporting chemical)***

In a DNA repair assay, *Salmonella typhimurium* strains TA1978 uvrB<sup>+</sup> and TA1538 uvrB<sup>-</sup> and *Escherichia coli* strains WP2 uvrA<sup>+</sup> recA<sup>+</sup> and WP100 uvrA<sup>-</sup> were exposed to rerun tower overheads at 10 µL/plate with and without metabolic activation. Positive and negative controls were included. The treatment caused weak differential killing in DNA repair deficient strains, *Escherichia coli* WP100 and *Salmonella typhimurium* TA1538 in the absence of metabolic activation, suggesting that rerun tower overheads can cause direct acting damage to bacterial DNA.

**Rerun tower overheads induced DNA damage in this assay.**

## ***Additional Information***

### ***Skin Irritation***

#### ***Gases (petroleum) light steam-cracked, butadiene conc. (CASRN 68955-28-2 containing ~67% 1,3-butadiene, supporting chemical)***

Two New Zealand White rabbits (1/sex) were administered 0.1 mL of gases (petroleum) light steam-cracked, butadiene conc. (~67% 1,3-butadiene, 30% butanes and 2% 1,2-butadiene) were administered 0.1 mL of gases (petroleum) light steam-cracked, butadiene conc. to the skin of both rabbits under occluded conditions (rubber dam). The test sites were evaluated 1, 3 and 7 days after dosing. The treated skin sites were virtually free of irritation at all observation intervals.

**Gases (petroleum) light steam-cracked, butadiene conc. was not irritating to the skin of rabbits in this study.**

### ***Eye Irritation***

#### ***Gases (petroleum) light steam-cracked, butadiene conc. (CASRN 68955-28-2 containing ~67% 1,3-butadiene, supporting chemical)***

Two New Zealand white rabbits (1/sex) were administered 0.1 mL of gases (petroleum) light steam-cracked, butadiene conc. (approximately 67% 1,3-butadiene, 30% butanes and 2% 1,2-butadiene) in one eye each and the untreated eye served as the control. Irritation was scored at 24, 48 and 72 hours. The eye irritation scores were 0 at all observation intervals.

**Gases (petroleum) light steam-cracked, butadiene conc. was not irritating to the eyes of rabbits in this study.**

### ***Carcinogenicity***

#### ***1,3 Butadiene (CASRN 106-99-0, > 99% purity, supporting chemical)***

(1) In an NTP study, B6C3F1 mice (50/sex/concentration) were exposed to 1,3-butadiene gas via inhalation at 0, 625 or 1250 ppm, 6 hours/day, 5 days/week. The study was scheduled to last 2 years but, was terminated at 60 (males) and 61 weeks (females) because of high mortality in both exposure groups. Survival was markedly reduced in exposed animals due primarily to malignant tumors. Increased incidences and early induction of hemangiosarcomas of the heart, malignant lymphomas, alveolar/bronchiolar adenomas and carcinomas, and papillomas of the stomach in males and females were seen. In addition, in females, acinar cell carcinomas of the mammary gland, granulose cell tumors of the ovary, hepatocellular adenomas and adenomas or carcinomas (combined) were seen. 1,3-Butadiene was associated with nonneoplastic lesions in the respiratory epithelium, liver necrosis, and testicular or ovarian atrophy.

(<http://ntp.niehs.nih.gov/?objectid=07074D99-988C-7FFE-D86FEB78BDADDE41>)

**1,3-Butadiene increased incidences of various tumors at multiple sites in this assay.**

(2) Sprague-Dawley rats (110/sex/concentration) were exposed to 1,3-butadiene gas via inhalation at concentrations of 0, 1000 or 8000 ppm, 6 hours/day, 5 days/week for 105 – 110 weeks. Significantly increased incidences of mammary gland tumors, Zymbal gland carcinomas, follicular cell tumors of the thyroid gland and uterine stromal carcinomas in females

and increased incidences of Leydig cell tumors and pancreatic exocrine tumors in males were observed. (IISRP, 2000; See human health data at [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/butadienereport019.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/butadienereport019.pdf)).

**1,3-Butadiene increased incidences of various tumors at multiple sites in this assay.**

(3) In two NTP studies, B6C3F1 mice (50 – 70/sex/dose) were exposed to 1,3-butadiene as a gas at concentrations of 6.25 – 1250 ppm for 6 hours/day, 5 days/week for up to 2 years. Treatment-related effects included increased incidences and early induction of hemangiosarcomas of the heart, malignant lymphomas, alveolar/bronchiolar carcinomas, squamous cell carcinomas of the stomach, acinar cell carcinomas of the mammary gland, malignant granulosa cell tumors of the ovary, hepatocellular adenomas and carcinomas (combined), histiocytic sarcomas and adenoacanthomas. [Details were obtained from NTP studies C50602A and C50602C. See NTP TR-434].

**1,3-Butadiene was carcinogenic to mice in these studies.**

(4) There is “sufficient evidence” from epidemiologic studies of exposed workers to consider 1,3-butadiene carcinogenic to humans. (<http://www.epa.gov/iris/subst/0139.htm>) IARC concluded that 1,3-butadiene is probably carcinogenic to humans [Group IA; (<http://monographs.iarc.fr/ENG/Monographs/vol54/mono54-11.pdf>)].

***Benzene (CASRN 71-43-2, supporting chemical)***

(1) In a NTP study, haploinsufficient p16<sup>Ink4a</sup>/p19<sup>Arf</sup> mice (15/sex/dose) were administered benzene in corn oil via gavage at 0, 25, 50, 100 or 200 mg/kg-bw, 5 days/week for 27 weeks. The incidence of malignant lymphoma was significantly increased in males at 200 mg/kg-bw. [Details were obtained from NTP study C99034: [http://ntp-apps.niehs.nih.gov/ntp\\_tox/index.cfm?fuseaction=ntpsearch.searchhome](http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchhome)].

**Benzene was carcinogenic to mice in this study.**

(2) In an NTP study, F344/N rats (50/sex/dose) were administered benzene in corn oil via gavage at 0, 25, 50 or 100 mg/kg-bw, 5 days/week for 103 weeks. Treatment-related increases were observed in the incidences of Zymbal gland carcinomas, squamous cell papillomas and carcinomas of the oral cavity and squamous cell papillomas and carcinomas of the skin (males only). [Details were obtained from NTP study C55276: [http://ntp-apps.niehs.nih.gov/ntp\\_tox/index.cfm?fuseaction=ntpsearch.searchhome](http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchhome)].

**Benzene was carcinogenic to rats in this study.**

(3) In an NTP study, B6C3F1 mice (50/sex/dose) were administered benzene in corn oil via gavage at 0, 25 (females only), 50, 100 or 200 (males only) mg/kg-bw, 5 days/week for 103 weeks. Exposure to benzene increased the incidences of Zymbal gland squamous cell carcinomas, malignant lymphomas, alveolar/bronchiolar carcinomas, squamous cell carcinomas of the preputial gland, ovarian granulosa cell tumors and carcinomas and carcinosarcomas of the mammary gland. [Details were obtained from NTP study C55276: [http://ntp-apps.niehs.nih.gov/ntp\\_tox/index.cfm?fuseaction=ntpsearch.searchhome](http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm?fuseaction=ntpsearch.searchhome)].

**Benzene was carcinogenic to mice in this study.**

(4) Benzene is characterized as a known human carcinogen for all routes of exposure based upon convincing human evidence as well as supporting evidence from animal studies (<http://www.epa.gov/ncea/iris/subst/0276.htm>).

### *Other*

#### ***1,3-Butadiene (CASRN 106-99-0, supporting chemical)***

(1) In the sperm head morphology assay, B6C3F1 mice (20 males/concentration) were exposed to 1,3-butadiene gas (purity 99.88%) via inhalation at concentrations of 0, 200, 1000 or 5000 ppm for 6 hours/day for 5 days and observed for up to five weeks post-exposure. Mice were sacrificed during the fifth post-exposure week and examined for lesions of the reproductive tract and other gross abnormalities. Sperms were obtained from the cauda of the right epididymis, slides were prepared and examined microscopically. The morphology of at least 500 sperm heads per mouse was categorized. There was 21, 73, and 129% increase in the abnormal sperm heads at 200, 1000 and 5000 ppm, respectively when compared to the controls. A statistical significance was achieved only for the values for the 1000 and 5000 ppm groups ( $p < 0.05$ ). Since only a single time-point was examined, the effect on all stages of spermatogenesis could not be determined. Mean body weights of 1,3-butadiene-exposed groups were not significantly different from the control value. (Morrissey, R.E., et al., Environ. Health Perspect. 86, 79-84.)

(2) In a rodent dominant lethal test, CD-1 Swiss mice (20 males/concentration) were exposed to 1,3-butadiene gas (purity 99.88%) via whole-body inhalation at concentrations of 0, 200, 1000 or 5000 ppm 6 hours/day for 5 consecutive days. After 5 days of exposure, the male mice were mated with unexposed females. Females were removed from cohabitation after 7 days, sacrificed 12 days later and the uterine contents examined. 1,3-Butadiene caused an increase in the percentage of females with two or more dead implants in all exposure groups in the first week following exposure. During the first week, there was a small but statistically significant increase in the number of dead implantations per pregnancy only at 1000 ppm (1.42 per pregnancy vs 0.78 in control). During the second week, there was a statistically significant increase in the number of dead implantations per pregnancy at 200 and 1000 ppm but not at 5000 ppm. These increases were due to increases in early deaths. No firm conclusions with regard to germ cell mutagenicity can be drawn. However, the study authors indicated that these results indicate possible adverse effects on mature cells.

**LOAEC = 200 ppm** (based on increased percentage of females with more than two dead implants and number of dead implantations per pregnancy)

**NOAEC = Not established**

(3) In a longer exposure dominant lethal test, male CD-1 mice (50/concentration) were exposed to 1,3-butadiene gas (purity >99.7%) via inhalation at concentrations of 0, 12.5, 65 or 130 ppm 6 hours/day, 5 days/week for 4 weeks. They were then mated with unexposed females. The pregnant females were killed and examined at 17 of gestation. The uteri were examined for live/dead fetuses, early and late deaths and malformed fetuses. There were no treatment-related mortalities. Body weights, mating frequency, pregnancy rates, period of coition and number of implantation sites were not affected. There was a statistically significant increase ( $p < 0.01$ ) in early deaths per implantation per pregnancy at 65 and 130 ppm. The number of early deaths at

12.5 ppm was not increased. There was no effect on late deaths. There were two runts in two litters in controls and at 12.5 ppm; one runt at 65 ppm and 6 runts in 5 litters at 130 ppm. Macroscopic abnormalities in skeletal structure were observed at all dose levels. Skeletal examination of abnormal fetuses during the macroscopic examination showed increased frequency of abnormalities of many parts of the skeleton in the runts from males in all treatment groups compared with their normal litter mates or normal controls. Mating frequency, period of coition, pregnancy rates and post-implantation loss were comparable to controls. The number of implantation sites was reduced at 65 ppm, but the impact on reproductive toxicity was unclear as there were no post-implantation losses. Study details are from TSCATS (OTS0559090).

**LOAEC = 65 ppm** (based on early deaths)

**NOAEC = 12.5 ppm**

**Conclusion:**

For pyrolysis C3+ and pyrolysis C4+ category members, the acute oral and inhalation toxicity in rats is low and moderate, respectively and acute dermal toxicity in rabbits is low based on supporting chemicals' data. Supporting chemical, CASRN 68955-28-2 is not irritating to rabbit skin or eyes.

For pyrolysis C3+ and pyrolysis C4+ category members, the acute oral and inhalation toxicity in rats is low and moderate, respectively, and acute dermal toxicity in rabbits is low based on supporting chemicals' data. The supporting chemical, CASRN 68955-28-2, is not irritating to rabbit skin or eyes.

Repeated-exposure studies with the supporting chemical, CASRN 71-43-2 show that the hematopoietic system is the most sensitive indicator of toxicity. Mice exposed repeatedly for 13 weeks via vapor inhalation to CASRN 71-43-2, showed hematological effects [e.g. decreases in RBC and WBC counts, platelets, hemoglobin, hematocrit], thymic atrophy and testicular effects at 0.96 mg/L/day; the NOAEC for systemic toxicity is 0.1 mg/L/day. In a similar study in mice, designed to assess specific effects on hematology, exposure to CASRN 71-43-2 for 10 weeks resulted in increases in spleen weight, total nucleated cells per spleen and nucleated RBCs at 0.03 mg/L/day; the NOAEC is not established. Repeated inhalation exposure of rats to CASRN 71-43-2 showed a decrease in WBC counts and percentage of lymphocytes at 0.96 mg/L/day; the NOAEC for hematological effects on peripheral blood circulation is 0.096 mg/L/day. The NOAEC for repeated exposure to the supporting chemical, CASRN 106-99-0, gas to mice for 13 weeks, is 625 ppm based on mortality seen at 1250 ppm. In a 13-week repeated-exposure study with CASRN 106-99-0 gas, rats showed no adverse effects at the highest concentration tested; NOAEC for systemic toxicity is 8000 ppm (highest concentration tested).

Guideline reproductive toxicity studies are not available for CASRN 71-43-2; however, in the 13-week inhalation exposures in mice, adverse effects were observed on the male and female reproductive organs. The sperm head morphology assay in mice for the supporting chemical, CASRN 106-99-0 (administered as gas), showed concentration-related increases in the percentage of abnormal sperm heads following five days of inhalation exposure to gas at concentrations of 200 to 5000 ppm. A 5-day inhalation exposure to CASRN 106-99-0, supporting chemical (gas), to male mice (mated with untreated females) in the dominant lethal test caused increases in the number of dead implantations (early) at concentrations as low as

200 ppm; although a strict concentration-response relationship was not observed. In the longer-term (4-weeks) dominant lethal test, inhalation exposure of CASRN 106-99-0, supporting chemical (gas) to male mice (mated with untreated female mice) showed early deaths at 65 ppm; the NOAEC is 12.5 ppm.

In the prenatal developmental toxicity study in mice via inhalation (gas), the supporting chemical, CASRN 106-99-0 showed decreased maternal body weight gains and decreased fetal and placental weights with an increased incidence of fetal variations at and above 200 ppm; the NOAEC is 40 ppm. Rats showed maternal and developmental toxicity when exposed to CASRN 106-99-0 gas via inhalation at 200 ppm based on decreased maternal body weight gains and fetal growth retardation, respectively; the NOAEC is not established. In the prenatal developmental toxicity study via gavage, the supporting chemical CASRN 64741-74-8 caused abortions in rabbit does at 50 mg/kg-day; the NOAEL for maternal toxicity is 25 mg/kg-day and for developmental toxicity it is 50 mg/kg-day (highest dose tested).

CASRN 71-43-2 induced gene mutations in bacteria and sister chromatid exchange in human lymphocytes *in vitro* and in rat and mouse lymphocytes *in vivo*. CASRN 71-43-2 induced micronuclei in rats and mice *in vivo*. The supporting chemical, CASRN 68955-28-2, was mutagenic in mammalian cells *in vitro* (but was not mutagenic in bacteria), induced chromosomal aberrations *in vivo* and induced unscheduled DNA synthesis *in vitro*. The supporting chemical, CASRN 68476-52-8, induced chromosomal aberrations *in vivo*. The supporting chemical, CASRN 106-99-0, was mutagenic in bacteria *in vitro* and induced chromosomal aberrations *in vivo*. The supporting chemical, CASRN 64741-74-8, was not mutagenic in bacteria *in vitro*; however, it was mutagenic in mammalian cells *in vitro* and caused DNA damage in bacteria in a DNA repair assay *in vitro*.

The supporting chemical, CASRN 71-43-2, is a known human carcinogen for all routes of exposure. The supporting chemical, CASRN 106-99-0, increased incidences of various tumors at multiple sites in rats and mice and there is “sufficient evidence” from epidemiologic studies of exposed workers to consider CASRN 106-99-0 carcinogenic to humans.

**Table 6. Summary of the Screening Information Data Set under the U.S. HPV Challenge Program - Human Health Data - Pyrolysis C3+ and Pyrolysis C4+ Category**

Endpoints	SPONSORED CHEMICAL Pyrolysis C3+ and Pyrolysis C4+ Streams  (64742-83-2, 68513-68-8)	SUPPORTING CHEMICAL Gases (pet.) light steam cracked, butadiene conc  (68955-28-2)	SUPPORTING CHEMICAL Hydrocarbons, C4, ethylene manufactured by- product (6847-52-8)	SUPPORTING CHEMICAL 1,3-Butadiene  (106-99-0)	SUPPORTING CHEMICAL Dripolene- Pyrolysis gasoline stream  (No CASRN)	SUPPORTING CHEMICAL Hydrotreated C <sub>6-8</sub> fraction (hydrogenated pyrolysis gasoline) (68410-97-9)	SUPPORTING CHEMICAL C <sub>5-10</sub> Fraction pyrolysis gasoline (Rerun Tower Overheads) (64741-74-8)	SUPPORTING CHEMICAL Benzene  (71-43-2)
Acute Oral Toxicity LD <sub>50</sub> (mg/kg)	No Data >810 – 10,000 (RA)	–	–	–	>2000	5170	>2000	>810 – 10,000
Acute Inhalation Toxicity LC <sub>50</sub> (mg/L)	No Data 43.7 (RA)	>5.3	–	129,000 ppm	–	12,408 ppm	–	43.7
Acute Dermal Toxicity LD <sub>50</sub> (mg/kg)	No Data >2000 (RA)	–	–	–	>2000	–	>2000	–
Repeated-Dose Toxicity NOAEC/LOAEC Inhalation (ppm/day)	No Data (Rat) 8000  (Mouse) NOAEC = Not Established LOAEC = 0.03 mg/L/day (RA)	(rat) 11,140 (highest concentration tested)	(rat) 20 mg/L/day (highest concentration tested)	(rat) 8000 (highest concentration tested)  (mouse) NOAEC = 625 LOAEC =1250	–	–	–	(mouse) (10 wks) NOAEC = Not Established LOAEC = 0.03 mg/L/day  (mouse) (13 wks) NOAEC = 0.1 mg/L/day LOAEC = 0.96 mg/L/day

**Table 6. Summary of the Screening Information Data Set under the U.S. HPV Challenge Program - Human Health Data - Pyrolysis C3+ and Pyrolysis C4+ Category**

<b>Endpoints</b>	<b>SPONSORED CHEMICAL Pyrolysis C3+ and Pyrolysis C4+ Streams  (64742-83-2, 68513-68-8)</b>	<b>SUPPORTING CHEMICAL Gases (pet.) light steam cracked, butadiene conc  (68955-28-2)</b>	<b>SUPPORTING CHEMICAL Hydrocarbons, C4, ethylene manufactured by- product (6847-52-8)</b>	<b>SUPPORTING CHEMICAL 1,3-Butadiene  (106-99-0)</b>	<b>SUPPORTING CHEMICAL Dripolene- Pyrolysis gasoline stream  (No CASRN)</b>	<b>SUPPORTING CHEMICAL Hydrotreated C<sub>6-8</sub> fraction (hydrogenated pyrolysis gasoline) (68410-97-9)</b>	<b>SUPPORTING CHEMICAL C<sub>5-10</sub> Fraction pyrolysis gasoline (Rerun Tower Overheads) (64741-74-8)</b>	<b>SUPPORTING CHEMICAL Benzene  (71-43-2)</b>
<b>Reproductive Toxicity NOAEC/LOAEC Inhalation (ppm/day)</b>  <b>Reproductive Toxicity</b>	No Data (mouse – 28-day) NOAEC = 12.5 LOAEC = 65  (mouse – 2-year) NOAEC(f) = Not Established LOAEC = 6.25 NOAEC(m) = 200 LOAEC (m) = 625  (rat) NOAEC = 13.3 mg/L/day (RA)	–	(rat) 20 mg/L/day (highest concentration tested)	(mouse – 28-day) NOAEC = 12.5 LOAEC = 65  (mouse – 2-year) NOAEC(f) = Not Established LOAEC(f) = 6.25 NOAEC(m) = 200 LOAEC (m) = 625  (rat) NOAEC = 13.3 mg/L/day (highest concentration tested)	–	–	–	13-week inhalation exposures in mice showed effects on testes and ovaries at 0.96 mg/L/day (highest concentration tested)
<b>Developmental Toxicity NOAEC/LOAEC Inhalation (mg/L/day)</b>  <b>Maternal Toxicity</b>  <b>Developmental Toxicity</b>	No Data (Rat) NOAEC = Not Established LOAEC =200 ppm  NOAEC = Not Established LOAEC =200 ppm	–	(rat) NOAEC = 20 (highest concentration tested)  NOAEC = 20 (highest concentration tested)	(rat) NOAEC = Not Established LOAEC =200 ppm  NOAEC = Not Established LOAEC =200 ppm	–	–	–	(rat) NOAEC = 0.96 (highest concentration tested)  NOAEC = 0.096 LOAEC = 0.96

**Table 6. Summary of the Screening Information Data Set under the U.S. HPV Challenge Program - Human Health Data - Pyrolysis C3+ and Pyrolysis C4+ Category**

<b>Endpoints</b>	<b>SPONSORED CHEMICAL Pyrolysis C3+ and Pyrolysis C4+ Streams  (64742-83-2, 68513-68-8)</b>	<b>SUPPORTING CHEMICAL Gases (pet.) light steam cracked, butadiene conc  (68955-28-2)</b>	<b>SUPPORTING CHEMICAL Hydrocarbons, C4, ethylene manufactured by- product (6847-52-8)</b>	<b>SUPPORTING CHEMICAL 1,3-Butadiene  (106-99-0)</b>	<b>SUPPORTING CHEMICAL Dripolene- Pyrolysis gasoline stream  (No CASRN)</b>	<b>SUPPORTING CHEMICAL Hydrotreated C<sub>6-8</sub> fraction (hydrogenated pyrolysis gasoline) (68410-97-9)</b>	<b>SUPPORTING CHEMICAL C<sub>5-10</sub> Fraction pyrolysis gasoline (Rerun Tower Overheads) (64741-74-8)</b>	<b>SUPPORTING CHEMICAL Benzene  (71-43-2)</b>
<b>Maternal Toxicity</b>	(rat) NOAEC = 0.96			(mouse) NOAEC = 40 ppm LOAEC = 200 ppm				(mouse) NOAEC = 0.064 (highest concentration tested)
<b>Developmental Toxicity</b>	NOAEC = 0.096 LOAEC = 0.96			NOAEC = 40 ppm LOAEC = 200 ppm				NOAEC = 0.032 LOAEC = 0.064
<b>Maternal Toxicity</b>	(mouse) NOAEC = 0.064							
<b>Developmental Toxicity</b>	(mouse) NOAEC = 0.032 LOAEC = 0.064 (RA)							
<b>Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-day) Maternal Toxicity</b>	No Data (rabbit) NOAEL = 25 LOAEL = 50	–	–	–	–	–	(Rabbit) NOAEL = 25 LOAEL = 50	–
<b>Developmental Toxicity</b>	NOAEL = 50 (RA)						NOAEL = 50 (highest dose tested)	
<b>Genetic Toxicity – Gene Mutation In vitro</b>	No Data Positive (RA)	Negative <sup>1</sup> Positive <sup>2</sup>	–	Positive	–	Negative	Negative <sup>1</sup> Positive <sup>2</sup>	Positive
<b>Genetic Toxicity – Gene Mutation In vivo</b>	No Data Negative (RA)	–	–	–	–	–	Negative	–

**Table 6. Summary of the Screening Information Data Set under the U.S. HPV Challenge Program - Human Health Data - Pyrolysis C3+ and Pyrolysis C4+ Category**

Endpoints	SPONSORED CHEMICAL Pyrolysis C3+ and Pyrolysis C4+ Streams  (64742-83-2, 68513-68-8)	SUPPORTING CHEMICAL Gases (pet.) light steam cracked, butadiene conc  (68955-28-2)	SUPPORTING CHEMICAL Hydrocarbons, C4, ethylene manufactured by- product (6847-52-8)	SUPPORTING CHEMICAL 1,3-Butadiene  (106-99-0)	SUPPORTING CHEMICAL Dripolene- Pyrolysis gasoline stream  (No CASRN)	SUPPORTING CHEMICAL Hydrotreated C <sub>6-8</sub> fraction (hydrogenated pyrolysis gasoline) (68410-97-9)	SUPPORTING CHEMICAL C <sub>5-10</sub> Fraction pyrolysis gasoline (Rerun Tower Overheads) (64741-74-8)	SUPPORTING CHEMICAL Benzene  (71-43-2)
Genetic Toxicity – Chromosomal Aberrations <i>In vivo</i>	No Data Positive (RA)	<b>Positive</b>	<b>Positive</b>	<b>Positive</b>	–	<b>Negative</b>	–	<b>Positive</b>
Genetic Toxicity – Other								
Unscheduled DNA Synthesis	–	<b>Positive</b>	–	–	–	<b>Positive</b>	–	–
DNA Damage	–	–	–	–	–	–	<b>Positive</b>	–
Additional Information								
Skin Irritation	–	<b>Not irritating</b>	–	–	–	–	–	–
Eye Irritation	–	<b>Not irritating</b>	–	–	–	–	–	–
Carcinogenicity	–	–	–	<b>Positive</b>	–	–	–	<b>Positive</b>

Measured data in bold text; (RA) = Read Across; (m) = male; (f) = female; – indicates that endpoint was not addressed for this chemical; <sup>1</sup>Tested in bacteria; <sup>2</sup>Tested in mammalian cells

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

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 7. The table also indicates where data for tested supporting chemicals are used to read-across (RA) for the untested members of the category.

##### *Acute Toxicity to Fish*

###### ***Benzene (CASRN 71-43-2, supporting chemical)***

(1) Rainbow trout (*Oncorhynchus mykiss*) were exposed to benzene at unspecified concentrations under flow-through conditions for 96 hours. Additional information can be found at [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf).

**96-h LC<sub>50</sub> = 5.3 mg/L**

(2) Bluegill sunfish (*Lepomis macrochirus*) were exposed to benzene at unspecified concentrations under static conditions for 96 hours. Additional information can be found at [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf).

**96-h LC<sub>50</sub> = 22.49 mg/L**

(3) Coho salmon (*Oncorhynchus kisutch*) were exposed to benzene at unspecified concentrations under static conditions for 96 hours. Additional information can be found at [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf).

**96-h LC<sub>50</sub> = 12.4 mg/L**

(4) Fathead minnow (*Pimephales promelas*) were exposed to benzene at unspecified concentrations under static conditions for 96 hours. Additional information can be found at [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf).

**96-h LC<sub>50</sub> = 12.6 mg/L**

###### ***Pentane (CASRN 109-66-0, supporting chemical)***

Rainbow trout (*Oncorhynchus mykiss*) were exposed to CASRN 109-66-0 for 96 hours. Additional information can be found at [http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/n-pentanereport043.pdf](http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/n-pentanereport043.pdf).

**96-h LC<sub>50</sub> = 4.26 mg/L**

###### ***2-Butene, 2-methyl- (CASRN 513-35-9, supporting chemical)***

Rainbow trout (*Oncorhynchus mykiss*) were exposed to CASRN 513-35-9 at nominal concentrations of 0, 2.13, 4.7, 10.3, 22.7 or 50 mg/L under static renewal conditions for 96 hours. Mean measured concentrations were 0, 1.67, 2.93, 5.33, 8.51 and 25.9 mg/L. Mortality was observed at concentrations  $\geq 5.33$  mg/L. One hundred percent mortality was observed

at  $\geq 8.51$  mg/L. Additional information can be found at  
<http://www.chem.unep.ch/irptc/sids/OECDSEIDS/513359.pdf>.  
**96-h LC<sub>50</sub> = 4.99 mg/L**

***Ethylene (CASRN 74-85-1)***

No acute toxicity data to fish is available for CASRN 74-85-1. ECOSAR (v. 1.00a) was used to estimate toxicity.

**96-h LC<sub>50</sub> = 95.7 mg/L**

***Acute Toxicity to Aquatic Invertebrates***

***Benzene (CASRN 71-43-2, supporting chemical)***

*Daphnia magna* were exposed to CASRN 71-43-2 for 48 hours. Additional information can be found at: [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf).

**48-h EC<sub>50</sub> = 10 mg/L**

***Pentane (CASRN 109-66-0, supporting chemical)***

*Daphnia magna* were exposed to CASRN 109-66-0 for 48 hours. Additional information can be found at: [http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/n-pentanereport043.pdf](http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/n-pentanereport043.pdf).

**48-h EC<sub>50</sub> = 2.7 mg/L**

***2-Butene, 2-methyl- (CASRN 513-35-9, supporting chemical)***

*Daphnia magna* were exposed to CASRN 513-35-9 at nominal concentrations of 2.13, 4.7, 10.3, 22.7 or 50 mg/L under static conditions for 48 hours. Mean measured concentrations were 0.691, 1.74, 2.95, 6.63 and 23.6 mg/L.

(<http://www.chem.unep.ch/irptc/sids/OECDSEIDS/513359.pdf>).

**48-h EC<sub>50</sub> = 3.84 mg/L**

***Ethylene (CASRN 74-85-1)***

No acute toxicity data for aquatic invertebrates is available for CASRN 74-85-1. ECOSAR (v. 1.00a) was used to estimate toxicity.

**48-h EC<sub>50</sub> = 48.4 mg/L**

***Toxicity to Aquatic Plants***

***Benzene (CASRN 71-43-2, supporting chemical)***

Green algae (*Pseudokirchneriella subcapitata*) were exposed to CASRN 71-43-2 for 72 hours. Additional information can be found at: [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf)

**72-h EC<sub>50</sub> = 28 mg/L (biomass)**

***Pentane (CASRN 109-66-0, supporting chemical)***

Green algae (*Pseudokirchneriella subcapitata*) were exposed to CASRN 109-66-0 for 72 hours. Additional information can be found at: [http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/n-pentanereport043.pdf](http://ecb.jrc.it/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/n-pentanereport043.pdf).

**72-h EC<sub>50</sub> = 7.5 mg/L (biomass)**

**72-h EC<sub>50</sub> = 10.7 mg/L (growth rate)**

***2-Butene, 2-methyl- (CASRN 513-35-9, supporting chemical)***

Green algae (*Pseudokirchneriella subcapitata*) were exposed to CASRN 513-35-9 at nominal concentrations of 0, 3.20, 7.04, 15.5, 34.1 and 75.0 mg/L for 96 hours. Mean measured concentrations were 0, 0.689, 1.53, 3.61, 7.22 and 21.1 mg/L. Additional information can be found at: <http://www.chem.unep.ch/irptc/sids/OECD/SIDS/513359.pdf>.

**72-h EC<sub>50</sub> = 10.5 mg/L (biomass)**

**72-h EC<sub>50</sub> = 12.0 mg/L (growth rate)**

***Ethylene (CASRN 74-85-1, supporting chemical)***

Green algae (*Pseudokirchneriella subcapitata*) were exposed to CASRN 74-85-1 at nominal concentrations of 8.2 – 131 mg/L for 72 hours. Mean measured concentrations were 3.3, 7.8, 13.9, 32 and 58 mg/L. Growth inhibition was observed at concentrations  $\geq$  32 mg/L. During the 72 hr exposure period there was a loss of ethylene in the range of 64-91 %, however in calculation of results the mean measured ethylene concentration was used. Additional information can be found at: <http://www.chem.unep.ch/irptc/sids/OECD/SIDS/74851.pdf>.

**72-h EC<sub>50</sub> (biomass) = 40 mg/L**

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

***Chronic Toxicity to Fish***

***Benzene (CASRN 71-43-2, supporting chemical)***

Fathead minnow (*Pimephales promelas*) were exposed to CASRN 71-43-2. Additional information can be found at: [http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK\\_ASSESSMENT/REPORT/benzenereport063.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/benzenereport063.pdf)

**32-d NOEC = 0.8 mg/L**

**Conclusion:** Based on the supporting chemicals, the 96-h LC<sub>50</sub> for fish is 4.26 mg/L (CASRN 109-66-0), the 48-h EC<sub>50</sub> for aquatic invertebrates is 2.7 mg/L (CASRN 109-66-0), and the 72-h EC<sub>50</sub> for aquatic plants ranges from 7.5 (CASRN 513-35-9) to 40 mg/L (CASRN 74-85-1) for biomass and 10.7 (CASRN 109-66-0) to 72 mg/L (CASRN 74-85-1) for growth rate. The chronic 32-d NOEC fish toxicity value is 0.8 mg/L (CASRN 71-43-2).

**Table 7. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program –Aquatic Toxicity Data**

<b>Endpoints</b>	<b>SUPPORTING CHEMICAL Ethylene (74-85-1)</b>	<b>SPONSORED CHEMICAL Pyrolysis C3+ (64742-83-2, 68513-68-8)</b>	<b>SPONSORED CHEMICAL Pyrolysis C4+ (64742-83-2)</b>	<b>SUPPORTING CHEMICAL 2-Butene, 2-methyl- (513-35-9)</b>	<b>SUPPORTING CHEMICAL n-Pentane (109-66-0)</b>	<b>SUPPORTING CHEMICAL Benzene (71-43-2)</b>
<b>Fish 96-h LC<sub>50</sub> (mg/L)</b>	-	No Data 4.26 (RA)	No Data 4.26 (RA)	<b>4.99</b>	<b>4.26</b>	<b>5.3</b>
<b>Aquatic Invertebrates 48-h EC<sub>50</sub> (mg/L)</b>	-	No Data 2.7 (RA)	No Data 2.7 (RA)	<b>3.84</b>	<b>2.7</b>	<b>10</b>
<b>Aquatic Plants 72-h EC<sub>50</sub> (mg/L)</b>		No Data	No Data			
<b>Biomass</b>	<b>40</b>	10.5 – 40	10.5 – 40	<b>10.5</b>	<b>7.5</b>	<b>28</b>
<b>Growth rate</b>	<b>72</b>	7.5 – 72 (RA)	7.5 – 72 (RA)	<b>12</b>	<b>10.7</b>	-
<b>Fish ChV (mg/L)</b>	-	No Data 0.8 (RA)	No Data 0.8 (RA)	-	-	<b>0.8</b> <b>(32-d NOEC)</b>

**bold** = experimental data; (e) = estimated data (i.e., derived from modeling); (RA) = Read-Across; – indicates that endpoint was not addressed for this chemical

## Appendix

The following pages show:

- Table 8—TSCA Definitions
- Ethylene Process Description and Process Streams
- Flow Diagram from the Ethylene Manufacturing Process Unit for the Pyrolysis C3+ and Pyrolysis C4+ Streams (taken from test plan;  
<http://www.epa.gov/oppt/chemrtk/pubs/summaries/olefins/c12064tc.htm>)

**Table 8. TSCA Definitions as provided by US EPA**

CASRN	Chemical Name	TSCA Definition
64742-83-2	Naphtha (petroleum), light steam-cracked	A complex combination of hydrocarbons obtained by the distillation of the products from a steam cracking process. It consists predominantly of unsaturated hydrocarbons having carbon numbers predominantly in the range of C4 through C11 and boiling in the range of approximately minus 20.degree.C to 190.degree.C (-4.degree.F to 374.degree.F). This steam is likely to contain 10 vol. % or more benzene. <sup>1</sup>
68476-52-8	Hydrocarbons, C4, ethylene-manuf.-by-product	A complex combination of hydrocarbons produced by distillation of products from a cracking process in an ethylene plant. It consists predominantly of C4 hydrocarbons.
68955-28-2	Gases (petroleum), light steam-cracked, butadiene conc.	A complex combination of hydrocarbons produced by the distillation of products from a thermal cracking process. It consists of hydrocarbons having a carbon number predominantly of C4.

## ETHYLENE PROCESS DESCRIPTION

### A. Ethylene Process

#### 1. Steam Cracking

Steam cracking is the predominant process used to produce ethylene. Various hydrocarbon feedstocks are used in the production of ethylene by steam cracking, including ethane, propane, butane, and liquid petroleum fractions such as condensate, naphtha, and gas oils. The feedstocks are normally saturated hydrocarbons but may contain minor amounts of unsaturates. These feedstocks are charged to the coils of a cracking furnace. Heat is transferred through the metal walls of the coils to the feedstock from hot flue gas, which is generated by combustion of fuels in the furnace firebox. The outlet of the cracking coil is usually maintained at relatively low pressure in order to obtain good yields to the desired streams. Steam is also added to the coil and serves as a diluent to improve yields and to control coke formation. This step of the ethylene process is commonly referred to as “steam cracking” or simply “cracking” and the furnaces are frequently referred to as “crackers”.

Subjecting the feedstocks to high temperatures in this manner results in the partial conversion of the feedstock to olefins. In the simplest example, feedstock ethane is partially converted to ethylene and hydrogen. Similarly, propane, butane, or the hydrocarbon compounds that are associated with the liquid feedstocks are also converted to ethylene. Other valuable hydrocarbons are also formed, including other olefins, diolefins, aromatics, paraffins, and lesser amounts of acetylenes. These other hydrocarbon streams include compounds with two or more carbon (C) atoms per molecule, i.e., C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, etc. Propane and propylene are examples of C<sub>3</sub> hydrocarbons and benzene, hexene, and cyclohexane are a few examples of the C<sub>6</sub> hydrocarbons.

The intermediate stream that exits the cracking furnaces (i.e., the furnace effluent) is forwarded to the finishing section of the ethylene plant. The furnace effluent is commonly referred to as “cracked gas” and consists of a mixture of hydrogen, methane, and various hydrocarbon compounds with two or more carbon atoms per molecule (C<sub>2</sub>+). The relative amount of each constituent in the cracked gas varies depending on what feedstocks are cracked and cracking process variables. Cracked gas may also contain relatively small concentrations of organic sulfur compounds that were present as impurities in the feedstock or were added to the feedstock to control coke formation. The cracked gas stream is cooled, compressed and then separated into the individual streams of the ethylene process. These streams can be sold commercially and/or put into further steps of the process to produce additional materials. In some ethylene processes, a liquid fuel oil stream is produced when the cracked gas is initially cooled. The ethylene process is a closed process and the streams are contained in pressurized systems (see Figure 2 for a pictorial representation of the ethylene manufacturing process). The final streams from the ethylene process include hydrogen, methane (frequently used as fuel), and the high purity chemicals, ethylene and propylene. Other streams from the ethylene process are typically mixed streams that are isolated by distillation according to boiling point ranges. C<sub>4</sub> Crude Butadiene and Pyrolysis Gasoline are the two most common of these mixed streams.


## 2. Refinery Gas Separation

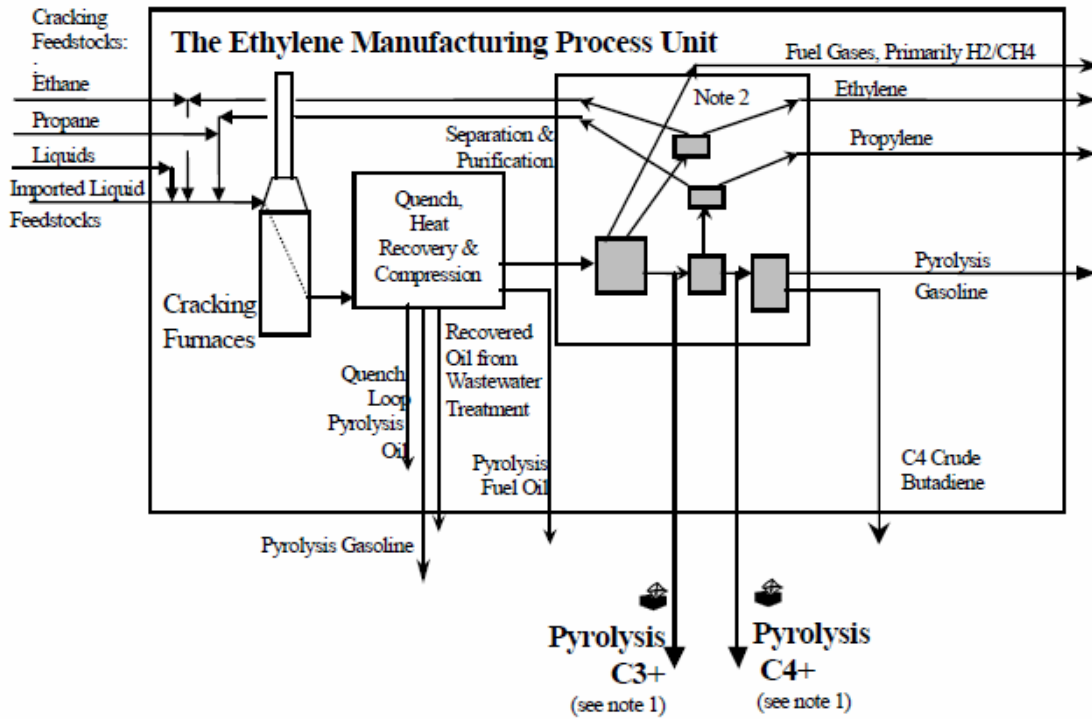
Ethylene and propylene are also produced by separation of these olefin streams, such as from the light ends product of a catalytic cracking process. This separation is similar to that used in steam crackers, and in some cases, both refinery gas streams and steam cracking furnace effluents are combined and processed in a single finishing section. These refinery gas streams differ from cracked gas in that the refinery streams have a much narrower carbon number distribution, predominantly C2 and/or C3. Thus, the finishing of these refinery gas streams yields primary ethylene and ethane, and/or propylene and propane.

### **B. Pyrolysis C3+ and Pyrolysis C4+ Category Streams**

The cracked gas from the ethylene process furnaces is cooled, compressed, and then separated into the desired product streams by a series of unit operations, primarily distillation. Pyrolysis C3+ is an intermediate stream in the separation sequence that results after removal of the C2 and lighter components from condensed cracked gas. The Pyrolysis C3+ is typically produced at the deethanizer tower bottoms. Similarly, Pyrolysis C4+ is the intermediate stream that is produced after removal of the C3 and lighter components, and is produced at the debutanizer tower bottoms. Infrequently, these two streams are temporarily isolated during ethylene process unit shutdowns. During normal operation, the Pyrolysis C4+ stream is separated by distillation into two streams, the butadiene containing C4 Crude Butadiene stream and pyrolysis gasoline (C5+). The Pyrolysis C3+ stream is separated into these two streams plus a C3 stream. The C3 stream (Propylene Streams Category) and pyrolysis gasoline (High Benzene Naphthas Category) are covered by separate categories sponsored by the Olefins Panel of the American Chemistry Council. There are only two examples where these broad-range streams are reported to be isolated. The 1,3-butadiene content of Pyrolysis C3+ and Pyrolysis C4+ streams can range from 12 to 42%.

**Process Streams Flow Diagram from the Ethylene Manufacturing Process Unit for  
the Pyrolysis C3+ and Pyrolysis C4+ Streams  
(as presented in the Test Plan)**

The Pyrolysis C3+ and Pyrolysis C4+ Category streams are shown in bold in the diagram below and marked . Other streams are shown for clarity.



Note 1: Pyrolysis C3+ & C4+ are typically in-process streams; the streams have been reported as isolated (rare) during process unit shutdowns.  
Note 2: Separation sequence shown is typical. Other sequences are used.