Chemical Name: Crude Butadiene C4 Category
Submitter: ACC

Chemicals in Category

CHEMICAL NAME	CASRN
1,3-Butadiene	106-99-0
Butenes	25167-67-3
Distillate (Petroleum), Extractive C3-5	68477-41-8
Gases, (Petroleum) Light Steam Cracked, Butadiene Conc.	68955-28-2
Hydrocarbons, >C3	68476-44-8
Hydrocarbons C3 – C4 rich petroleum distillates	68512-91-4
Hydrocarbons, C4, Ethane-Propane Cracked	68187-60-0
Hydrocarbons, C4, Ethylene Manufactured By-Product	68476-52-8
Hydrocarbons C4, unsaturated	68956-54-7
Hydrocarbons, C4-7, Butadiene Manufactured By-Product	69103-05-5
Naphtha, (Petroleum), Light Steam-Cracked	64742-83-2
Residues (Petroleum), Deethanizer Tower	68513-68-8

As the Agency received data from High Production Challenge Program participants, it posted notice of and links to those data here for public review and comment. Companies and consortia were requested to defer any proposed new testing on their chemicals for a period of 120 days from when their Test Plans and Robust Summaries were posted to the Internet, in order to allow for technical public comment regarding the possible provision of additional existing data or other technical information which might address or eliminate the need for some new testing.

Some sponsors of chemicals submitted revised test plans and robust summaries to the Agency and referred to them as "final" submissions. EPA previously referred to the most recent submission as "revised" and has made no distinction or judgment whether a submission is final. Lastly, technical public comments on test plans and robust summaries were also provided for several chemicals/categories.

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The pdf contains the following documents:

HIGH PRODUCTION VOLUME (HPV)

CHEMICAL CHALLENGE PROGRAM

TEST PLAN

For The

CRUDE BUTADIENE C4 Category

Prepared by:

CMA Olefins Panel, HPV Implementation Task Group

May 1, 2000

PLAIN ENGLISH SUMMARY

This test plan addresses crude butadiene streams, which typically contain 10 to 92 percent 1,3-butadiene. Three substances will be evaluated: pure butadiene (already tested), a mid-range stream containing approximately 45-67 percent butadiene (also already tested), and a low concentration stream with approximately 10 percent butadiene (testing will be conducted). Based on existing data, the test sponsors believe the biological activity of each stream will be determined by the 1,3-butadiene content in the stream. These streams also contain other C4 substances. Additional data will be collected on these other substances, either under other test plans under the HPV Challenge Program, or through the OECD SIDS or ICCA program. The additional data will assist the test sponsors in determining whether 1,3-butadiene is the most biologically active component of the crude butadiene streams.

EXECUTIVE SUMMARY

The Chemical Manufacturers Association (CMA) Olefins Panel and its member companies hereby submit for review and public comment the test plan for the Crude Butadiene C4 category under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Chemical Challenge Program (Program). It is the intent of the CMA Olefins Panel and its member companies to use new information in conjunction with a variety of existing data and scientific judgment/analyses to adequately characterize the SIDS (Screening Information Data Set) human health, environmental fate and effects, and physicochemical endpoints for this category.

This test plan addresses crude butadiene streams. Streams are mixtures of chemicals. In the case of crude butadiene streams, they are mixtures of butadiene and other chemicals, primarily chemicals containing 4 carbons. The major difference between the different crude butadiene streams is the amount of the various chemicals in the streams. Because butadiene is believed to be the most toxic chemical in the mixture, the strategy is to evaluate streams containing different concentrations of butadiene, covering the range of butadiene concentration found in these streams.

Crude butadiene streams typically contain 10 to 92 percent 1,3-butadiene, with the balance consisting predominantly of other C4 substances including 1-butene, 2-butene, isobutylene, butane and isobutane. The plan advocates addressing the category by evaluating three substances: pure butadiene (data already available), a mid-range stream containing approximately 45-67 percent butadiene (data already available), and a low concentration stream with approximately 10 percent butadiene (testing will be conducted). 1,3-Butadiene has been extensively studied and is in the SIDS process. The SIDS review is expected to be completed by the end of 2000. The test plan is based on the expectation that the presence of butadiene in the crude butadiene C4 streams will be responsible for the biological activity of the streams. This assumption is based in part on 1,3-butadiene data, and also on what is known about the other C4 compounds. Additional data will be collected on other C4 compounds as part of other test plans under the HPV Challenge Program, the ICCA program, or from chemicals already sponsored in the OECD SIDS program. The additional data will assist the Panel in determining whether butadiene is the most biologically active component of the Crude Butadiene C4 streams.

One crude butadiene stream is the full range butadiene concentrate. This stream is a mixture of butadiene, other chemicals containing 4 carbons, and other chemicals with fewer than or more than 4 carbons. Benzene is a significant component of the full range butadiene concentrate. The complete characterization of the full range butadiene concentrate stream will be accomplished by use of data from this test plan along with data from other Olefins

Panel categories (including a category with streams containing benzene) and from the data on benzene itself, which is in the SIDS process.

Predictive computer models will be used to develop much of the aquatic toxicity, environmental fate, and physicochemical data for substances in the Crude Butadiene C4 category. Aquatic toxicity testing procedures were not designed for gaseous substances like those in this category and testing will not be conducted. However, relevant information will be provided in a technical discussion that addresses the physical nature of these substances and includes a discussion of calculated aquatic toxicity data. The calculated data will be developed from a computer model used by the EPA. Relevant environmental fate information will be summarized either through the use of computer models when meaningful data can be developed or in technical discussions when computer modeling is not applicable. Physicochemical properties will be represented as a range of values according to component composition. These data will be calculated using a computer model cited in an EPA guidance document prepared for the HPV Challenge Program.

LIST OF MEMBER COMPANIES
THE OLEFINS PANEL

The Chemical Manufacturers Association (CMA) Olefins Panel includes the following member companies:

BP Amoco, p.l.c.
Chevron Chemical Company LLC
CONDEA Vista Company
The Dow Chemical Company
E. I. du Pont de Nemours and Company
Eastman Chemical Company
Equistar Chemicals, LP
ExxonMobil Chemical Company
Fina Oil and Chemical Company*
Formosa Plastics Corporation, U.S.A.
The B.F.Goodrich Company*
The Goodyear Tire & Rubber Company
Huntsman Corporation
Koch Industries*
NOVA Chemicals Inc.
Phillips Chemical Company
Shell Chemical Company
Sunoco, Inc.*
Texas Petrochemicals Corporation
Union Carbide Corporation
Westlake Chemical Corporation
Williams Olefins, LLC

* These companies are part of the Olefins Panel but do not produce CAS numbers in the Crude Butadiene C4 Category.

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TEST PLAN FOR THE CRUDE BUTADIENE C4 CATEGORY

TEST PLAN FOR THE CRUDE BUTADIENE C4 CATEGORY

I. INTRODUCTION

The Chemical Manufacturers Association (CMA) Olefins Panel (Panel) and its member companies have committed voluntarily to develop screening level human health effects, environmental effects and fate, and physicochemical test data for the Crude Butadiene C4 category under the Environmental Protection Agency's (EPA's) High Production Volume (HPV) Challenge Program (Program).

This plan identifies CAS numbers used to describe process streams in the category, identifies existing data of adequate quality for substances included in the category, and outlines testing planned to develop screening level data for this category under the Program. This document also provides the testing rationale for the Crude Butadiene C4 category. The objective of this effort is to identify and develop sufficient test data and/or other information to adequately characterize the human health and environmental fate for the category in compliance with the EPA HPV Program. Physicochemical data that are requested in this program will be calculated as described in EPA guidance documents.

II. DESCRIPTION OF THE CRUDE BUTADIENE C4 CATEGORY

A. The Category

The Crude Butadiene C4 Category was developed by grouping process streams that the Panel believes are similar from both a process and toxicology perspective. Twelve CAS numbers (Table 1) are used to describe these process streams. A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. Those mixtures containing 10 to 92% butadiene are referred to as "crude butadiene." With the exception of CAS 106-99-0 (which is pure 1,3-butadiene), the CAS numbers or streams in this category consist of complex mixtures of hydrocarbons. Most of the commercial products in this category have a carbon number distribution predominantly between C3 and C5. All these streams contain significant levels of 1,3-butadiene and olefins, which is why this group is considered a category for purposes of the HPV Program, and designated Crude Butadiene C4. The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is not uncommon to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process).

The crude butadiene streams arise from production processes associated with ethylene manufacturing. A description of the ethylene and associated processes is included in Appendix I. Briefly, the three process streams (sometimes referred to as products) are:

(1) Butadiene concentrate arises from the distillation of cracked gas. This typically contains 40% to about 60% 1,3-butadiene (table 2), but could contain between 10% and 80% butadiene. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons.

(2) High butadiene heavy ends from the butadiene plant that arise from extractive distillation. The 1,3-butadiene content of this mixed stream ranges from 13% to 92% (table 2). Other chemicals in this mixed stream are predominately chemicals containing 4 carbons.

(3) Full-range butadiene concentrate which is the mixed stream remaining after the removal of ethylene. The 1,3-butadiene content of full range butadiene concentrate has been reported to range from 12% to 42% (table 2). Other chemicals in this mixed stream are those containing three to twelve carbons.

Note that any of the CAS numbers in this category (except the CAS number for 1,3-butadiene itself) can be used correctly to describe any of the mixed streams discussed above.

III. TEST PLAN RATIONALE

A. Overview

1. Butadiene Concentrate and Heavy Ends

Much of existing data for the Crude Butadiene C4 category are for 1,3-butadiene (Table 3), the hydrocarbon substance which is likely the most biologically active of the substances in the category and thus the major contributor to toxicological activity. 1,3-Butadiene itself is in the SIDS process and the review is expected to be completed by the end of 2000. Because of the SIDS review, butadiene has, or should have in the future, existing data of adequate quality for each of the end points. A possible exception is the acute inhalation toxicity study. The acute toxicity study included in the robust summaries, which are submitted as a separate document, contained insufficient experimental detail to assess quality. However, 1,3-butadiene has been extensively studied and acute toxicity is clearly not an issue. Our understanding of the toxicity of 1,3-butadiene would not be improved by repeating the acute toxicity study. Therefore, it was decided that the existing study was sufficient to address the acute toxicity endpoint for 1,3-butadiene. There are also data available for two crude butadiene streams. The compositions of the two previously tested crude butadiene streams were: (1) 45% 1,3-butadiene, 20% butanes, and 30% butenes and (2) 67% 1,3-butadiene, 30% butenes, and 2% 1,2-butadiene. 1,3-Butadiene is present in all the CAS numbers in this category. The presence of this chemical at concentrations >10% by weight creates a presumption under the Program that the substance would result in positive genotoxicity as the most sensitive endpoint. Supporting this presumption, the crude butadiene feedstock containing 45% butadiene has

been shown to be genotoxic.

To verify the relevance of the extrapolation of 1,3-butadiene data to substances with lower 1,3-butadiene concentrations, a full SIDS human health test battery will be conducted for a process stream containing approximately 10% 1,3-butadiene. This process stream will also include other chemicals that are included in the other streams that make up this category. The exact composition of the stream to be tested will be determined analytically at the time of testing.

The data for 1,3-butadiene together with the data from the low (approximately 10%) 1,3-butadiene-containing process stream and the data from the mid-level (45-67%)1,3-butadiene streams will be sufficient to adequately characterize the range of substances included in the category and the associated potential human health effects under the HPV Program. Crude butadiene (full range) also contains benzene. It is anticipated that similar cytogenic effects (micronuclei induction, etc.) will result from benzene, based on knowledge of the existing SIDS data set for benzene. However, it is proposed to complete a full HPV SIDS test battery for a benzene-containing stream in the High Benzene Naphtha category (volunteered for testing in 2001). The information obtained from testing a High Benzene Naphtha stream will be used in conjunction with the information obtained from testing the Crude Butadiene C4 stream described above to fully characterize the full range product.

Environmental fate and effects test data for the required endpoints do not exist for substances in this category (Table 3). This is not unexpected because these CAS numbers represent mixtures of gaseous substances and therefore, are not appropriate to be evaluated using existing standard testing guidelines. In addition, because these substances are gases, it is highly unlikely that they will pose a hazard to aquatic or terrestrial environments. As a result, aquatic toxicity and biodegradation testing will not be conducted based on the physical state of these substances and their physicochemical parameters (i.e., low boiling point, high volatility, and high Henry's Law constants). However, the environmental endpoints for photodegradation, hydrolysis, transport, and fugacity will be either calculated or discussed.

Structure-activity relationships (SARs) can be used to calculate transport (Koc) and fugacity, the latter of which is only calculated. Components of process streams in the category will partition primarily to the air, and because they have relatively low Kow values, their fate in air is the focus of environmental interest. In addition, these low Kow values suggest that they will not partition to suspended organic matter in air and therefore they will not precipitate to aquatic and terrestrial compartments.

In all cases, based on physicochemical characteristics, these substances will partition to the air at a rapid rate if released to the environment. As a result, the aquatic and terrestrial environments will not be the compartments of concern when evaluating the potential environmental impact of these substances. However, there are SARs that can be used to evaluate the potential toxicity of chemicals. A SAR will be used to calculate the toxicity of selected chemical components of the Crude Butadiene C4 category.

2. Full-Range Butadiene Concentrate

To completely characterize the toxicity of the full-range butadiene concentrate streams, data from the Crude Butadiene C4 category will be combined with data obtained during the assessment of other categories under the Olefins Panel's HPV program. Specifically, the data for the Crude Butadiene C4 category, the C-5 category, the High Benzene Naphtha category which contains benzene, and the C-3 streams category, which contains other 3 carbon compounds will, taken together, completely characterize the toxicity of this stream. Additionally, as noted, the available SIDS data sets on 1,3-butadiene and benzene will be used to assess two major determinants of toxicity of these streams.

B. Human Health Effects

1,3-butadiene (CAS #106-99-0) is likely the most biologically active component of the process streams in the Crude Butadiene C4 category. There are existing data for 1,3-butadiene, which is a SIDS listed material. The toxicity of other major components (primarily butanes and butenes), is known or will be known from current or planned testing to be sponsored by the Chemical Manufacturers Association and American Petroleum Institute. For more details on other test categories, see Section V - Other Relevant Data.

The toxicity of butadiene can be used to characterize the Crude Butadiene C4 streams represented by the CAS numbers in the category, because butadiene is typically present at greater than 10 percent. It is anticipated that positive genotoxicity will be the health effect endpoint most likely to show a positive response at the lowest test concentration for this category.

To confirm the relevance of the extrapolation of data from category members with high 1,3-butadiene content to process streams with a similar carbon number range but with lower butadiene content, a full test battery is recommended for a stream containing approximately 10% butadiene. The exact composition of the low 1,3-butadiene containing stream will be determined analytically at the time of testing. Health effects testing will be conducted by the inhalation route and will consist of the acute toxicity, Ames, mouse micronucleus, and combined repeat dose/reproductive effects/neurotoxicity screen. Of the SIDS endpoints, only the mouse micronucleus test is known to show a dose-related adverse response with butadiene exposure and with the exception of acute central nervous system effects, no other significant adverse effects have been identified in the SIDS testing conducted on other C4 substances. Additional data on other C4 components will become available through the SIDS, ICCA, and HPV programs to complete the data base for these compounds (see Section VI).

It is anticipated that the biological spectrum of activity for 1,3-butadiene, with regard to positive genotoxicity, may be reflected in the other process streams in the category. Since metabolism of butadiene is required for toxicity, and other C4 alkenes are metabolized through a common metabolic pathway, it is anticipated that mixed components will compete

for the same active enzyme sites. Different individual toxicities, which are dependent on the formation of biologically active metabolites, may be reduced, as less metabolite(s) will be produced through competition for these sites. Hence the positive genotoxicity of butadiene may in fact be reduced or eliminated by the greater presence of the other components. This is supported by existing test data for a feedstock stream containing 45% butadiene which appears to be less genotoxic than 1,3-butadiene per se. This will be further assessed by testing a stream containing a low concentration (approximately 10%) of 1,3-butadiene.

This recommended testing, in conjunction with existing data and data under development for selected components of the process streams covered by this category, will provide adequate data to characterize the Crude Butadiene C4 category for human health effects endpoints under the Program.

C. Ecotoxicity

There are three aquatic toxicity endpoints in the HPV Program:

- Acute Toxicity to Fish
- Acute Toxicity to Aquatic Invertebrates
- Toxicity to Algae (Growth Inhibition)

EPA identifies the following test methods to determine these endpoints: OECD Guideline 203, *Fish Acute Toxicity Test*; Guideline 202, *Daphnia sp., Acute Immobilization Test*; and Guideline 201, *Alga Growth Inhibition Test* [2].

The OECD aquatic toxicity test methods were not designed to assess the acute toxicity of gaseous substances like those in the Crude Butadiene C4 category. Therefore, the Panel will develop a Robust Summary Statement that addresses the physical nature of these substances and the fact that their primary route of loss will be to the air. This discussion will include calculated toxicity data for selected chemical components. The calculated data will be developed using ECOSAR, a SAR program found in EPIWIN [1].

D. Environmental Fate

Predictive models will be used to develop meaningful data for chemicals that are gaseous at relevant environmental temperatures and pressures. The environmental fate data include:

- Photodegradation
- Stability in Water (Hydrolysis)
- Transport and Distribution (Fugacity)
- Biodegradation

1. Photodegradation

Direct photochemical degradation occurs through the absorbance of solar radiation by a chemical substance. If the absorbed energy is high enough then the resultant excited state of the chemical may undergo a transformation. Simple chemical structures can be examined to determine whether a chemical has the potential for direct photolysis in water. First order reaction rates can be calculated for some chemicals that have a potential for direct photolysis using the procedures of Zepp and Cline [2].

Photodegradation can be measured [3] (EPA identifies OECD test guideline 113 as a test method) or estimated using models accepted by the EPA [4]. An estimation method accepted by the EPA includes the calculation of atmospheric oxidation potential (AOP). Atmospheric oxidation as a result of hydroxyl radical attack is not direct photochemical degradation, but rather indirect degradation. AOPs can be calculated using a computer model. Chemicals that are gases will be available for atmospheric oxidation reactions with photochemically generated hydroxyl radicals. This will be the most significant route of degradation in the environment for category members.

The computer program AOPWIN (atmospheric oxidation program for Microsoft Windows) [1] is used by OPPTS. This program calculates a chemical half-life based on an overall OH reaction rate constant, a 12-hr day, and a given OH concentration. This calculation will be performed for representative chemical components identified in the Crude Butadiene C4 category.

2. Stability in Water (Hydrolysis Testing and Modeling)

Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters [5]. Stability in water can be measured [3] (EPA identifies OECD test guideline 111 as a test method) or estimated using models accepted by the EPA [4]. An estimation method accepted by the EPA includes a model that can calculate hydrolysis rate constants for esters, carbamates, epoxides, halomethanes, and selected alkylhalides. The computer program HYDROWIN (aqueous hydrolysis rate program for Microsoft windows) [1] is used by OPPTS.

It will not be necessary to run the model for the components of the streams in this category because the model cannot estimate their hydrolysis rate. Instead, a technical discussion as to why these chemicals would not be subject to hydrolysis will be prepared.

3. Chemical Transport and Distribution In The Environment (Fugacity Modeling)

Fugacity based multimedia modeling can provide basic information on the relative distribution of chemicals between selected environmental compartments (i.e., air, soil, sediment, suspended sediment, water, biota). The US EPA has acknowledged that computer modeling techniques are an appropriate approach to estimating chemical partitioning (fugacity is a

calculated endpoint and is not measured). A widely used fugacity model is the EQC (Equilibrium Criterion) model [6]. EPA cites the use of this model in its document titled *Determining the Adequacy of Existing Data* [3], which was prepared as guidance for the HPV Program.

In its document, EPA states that it accepts Level I fugacity data as an estimate of chemical distribution values. The input data required to run a Level I model include basic physicochemical parameters; distribution is calculated as percent partitioned to 6 compartments within a unit world. Level I data are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical is likely to partition.

The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. This model will be used to calculate distribution values for representative chemical components identified in streams in this category. A computer model, EPIWIN - version 3.02 [1], will be used to calculate the properties needed to run the Level I EQC model.

4. Biodegradation Testing

Biodegradation is the utilization of a chemical by microorganisms as a source of energy and carbon. The parent chemical is broken down to simpler, smaller chemicals, which are ultimately converted to an inorganic form such as carbon dioxide, nitrate, sulfate, and water. Assessing the biodegradability of organic chemicals using a standard testing guideline can provide useful information for evaluating chemical hazard.

Substances in this category are gaseous at room temperature. Standard OECD biodegradation test methods were not designed to assess the relative biodegradability of gaseous materials. To provide relevant information for this endpoint, a discussion will be developed on the physical nature of these substances and the fact that their primary route of loss will be to the air compartment where they will degrade through hydroxyl radical attack, which is briefly described under *photodegradation* above.

E. Physicochemical Properties

The physicochemical properties include:

- Melting Point
- Boiling Point
- Vapor Pressure
- Octanol/Water Partition Coefficient
- Water Solubility

Because the HPV substances covered under the Olefins Crude Butadiene C4 category testing plan are variable mixtures, it is not possible to develop or calculate a single numerical value for some of the physicochemical properties. For example, a product that is a mixture of chemicals does not have a melting point, but rather a melting range. Values for physicochemical properties will be represented as a range of values according to the product's component composition and based on the results of computer modeling.

Data for the physicochemical endpoints will be developed using sources recommended by EPA. There are estimation models (Structure-Activity Relationships, SAR) for each of these endpoints in the EPIWIN [1] (Estimation Program Interface for Windows) computer program and EPA has indicated that it will accept estimated data using this program [4].

Boiling point, melting point, and vapor pressure ranges will be determined using the MPBPVP subroutine in EPIWIN. K_{ow} and water solubility will be calculated using KOWIN and WSKOW subroutines, respectively. There is more information on calculating data for the HPV chemical program in the EPA document titled, *The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program.*

IV. TEST PLAN SUMMARY

The following testing, modeling, and technical discussions will be developed for the Crude Butadiene C4 category (Table 3):

- Conduct one test battery for all SIDS human health endpoints on a product (stream) containing approximately 10% 1,3-butadiene (exact composition to be determined at the time of testing).
- Compare evaluated endpoints to those for 1,3-butadiene and the other identified data and prepare a technical discussion in terms of their representation of potential human health effects for this category.
- Prepare a technical discussion of the potential aquatic toxicity of selected chemical components comprising streams in this category using modeled data.
- Prepare a technical discussion on the potential of chemical components comprising streams in this category to photodegrade.
- Prepare a technical discussion on the potential of chemical components comprising streams in this category to hydrolyze.
- Prepare a technical discussion on the potential biodegradation of chemical components of streams in this category.
- Calculate fugacity data for selected chemical components of streams in this category.
- Calculate physicochemical data as described in the EPA document titled, *The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program.*

Summaries of results will be developed once the data and analyses are available. This test plan is expected to provide adequate data to characterize the human health effects and environmental fate and effects endpoints for the category under the Program.

V. OTHER RELEVANT DATA

The Crude Butadiene C4 test category addresses crude butadiene streams, which typically contain 10 to 92 percent 1,3-butadiene, with the balance consisting predominantly of other C4 substances including 1-butene, 2-butene, isobutylene, butane and isobutane. The plan proposes addressing the category using data for three substances: pure butadiene, a mid-range stream containing approximately 45-60 percent butadiene, and a low concentration stream with approximately 10 percent butadiene. The test plan is based on the expectation that the biological activity of 1,3-butadiene will be responsible for the effects seen in the testing of the crude butadiene streams. This assumption is based in part on 1,3-butadiene data, and also what is known about the other C4 compounds. Additional data will be collected on other components of these streams as part of other test plans under the HPV Challenge Program, the ICCA program, or from chemicals already sponsored in the OECD SIDS program.

Propane and propylene account for most of the C3 materials found in the crude butadiene streams. The Petroleum HPV Test Group, managed by API, has taken responsibility for propane under the HPV program. The data set for propylene is expected to be covered under the ICCA program.

Major C4 components other than 1,3-butadiene, commonly present in crude butadiene streams included butane, isobutane, 1-butene, isobutylene and 2-butene. The Petroleum HPV Test Group has taken responsibility for butane and isobutane. The CMA Olefins Panel will complete the data set for 1-butene as part of a separate test category (Category 2 Low butadiene C4). Isobutylene and 2-butene are already in the OECD SIDS program. Therefore, data already exists or will be developed for each of the major C4 components in the Crude Butadiene C4 category.

The full-range butadiene concentrate stream included in this test category consists of the entire C3+ or C4+ compounds produced in the cracking furnace. This stream is only rarely isolated and is usually site-limited. Normally this stream is further processed by distillation into a C3 fraction (propylene stream), a C4 fraction (C4 butadiene concentrate) and a C5+ fraction (pyrolysis gasoline). A separate test plan, sponsored by the CMA Olefins Panel, will be submitted for the C3 fraction. The C4 fraction is the material of primary interest in this test category. Testing of the C5+ fraction will be done under separate test categories sponsored by the CMA Olefins panel. More specifically, a separate test plan will be submitted for the C3 propylene stream, for the predominantly C5 category, for a C6+ high benzene naphtha category and for a low benzene naphtha category. For a complete list of test categories sponsored by the CMA Olefins Panel see table 4. It is also worth noting that in addition to 1,3-butadiene, many of the other major components found in the full-range butadiene

concentrate stream are in the OECD SIDS program including benzene, toluene and dicyclopentadiene. While testing a C3+ or C4+ stream is not specifically proposed, sufficient data will become available to characterize this material as a result of the testing of the various cuts previously mentioned.

REFERENCES

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Table 1. CAS Numbers And Descriptions.

CAS Number	CAS Number Description
106-99-0	1,3-Butadiene
25167-67-3	Butenes
68477-41-8	Distillate (Petroleum), Extractive C3-5
68955-28-2	Gases, (Petroleum) Light Steam Cracked, Butadiene Conc.
68476-44-8	Hydrocarbons, >C3
68512-91-4	Hydrocarbons C3 – C4 rich petroleum distillates
68187-60-0	Hydrocarbons, C4, Ethane-Propane Cracked
68476-52-8	Hydrocarbons, C4, Ethylene Manufactured By-Product
68956-54-7	Hydrocarbons C4, unsaturated
69103-05-5	Hydrocarbons, C4-7, Butadiene Manufactured By-Product
64742-83-2	Naphtha, (Petroleum), Light Steam-Cracked
68513-68-8	Residues (Petroleum), Deethanizer Tower

Table 2. Typical Composition Ranges (Percent) For Crude Butadiene Streams

Component	Crude Butadiene or Butadiene Concentrate	Heavy Ends	Full-Range Butadiene Concentrate
Tert-butyl catechol	0 - 0.01		
Methanol	0.0 - 0.3		
Propylene	0.0 - 1.9		0 - 4.0
Other C3 &lighter	0.5 - 1.7		0 - 1.0
Methylacetylene & Propadiene	0.0 - 2.3		
Ethyl & Vinylacetylene	0.7 - 3.0		
Isobutane	0.4 - 22		0.0 - 1.1
n-Butane	1.5 - 30	0.0 - 6.0	1.0 - 4.5
Isobutylene	0.5 - 29		5.0 - 12
cis & trans-butene-2	3.5 - 54	5 - 50	1.5 - 6.4
Butene-1	2.5 - 25	0.0 - 4.0	5.0 - 11
1,3-Butadiene	**10 - 82**	**13 - 92**	**12 - 42**
1,2-Butadiene	0.0 - 1.4	0.0 - 2.0	0.0 - 1.0
C5 & Higher	0.0 - 8.0		
Vinylcyclohexene	0.0 - 1.0		
Isopentane		0.0 - 3.0	
C8		0.0 - 4.0	
1,4-pentadiene			0.2 - 1.2
Pentene-1			0.5 - 2.3
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-aromatics			2.0 - 12
Benzene			11 - 42
Toluene			1.8 - 25
Xylenes			0.1 - 4.0
Ethylbenzene			0.1 - 1.3
Dicyclopentadiene			2.0 - 10
Indene			0.3 - 1.9
Naphthalene			0.2 - 1.6
Other C9 and higher			1.5 - 8.7

Note 1: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 highs and lows should not be considered absolute values for these limits. They are instead the highs and lows of the reported values, and are expected to be typical limit values.
Note 3: The definitions, found in the TSCA Chemical Substance Inventory, for the CAS numbers included in this group are vague with respect to composition. Therefore, it is not uncommon to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition).

Table 3. Assessment Plan For Crude Butadiene C4 Category Under The Program. Robust summaries for existing studies are submitted separately.

Product Description	Human Health Effects						Ecotoxicity			Environmental Fate				
	Acute Toxicity	Genetic Point Mut.	Genetic Chrom.	Sub-chronic	Develop-mental	Reproduc-tion	Acute Fish	Acute Invert.	Algal Toxicity	Physical Chem.	Photo-deg.	Hydro-lysis	Fugacity	Biodeg.
1,3-Butadiene	v	v	v	v	v	v[1]	NA	NA	NA	SAR	TD	TD	CM	TD
Mid-range 1,3-Butadiene- 67% 1,3-butadiene, 30% butenes, 2% 1,2-butadiene	RA	v	RA	RA	RA	RA	NA	NA	NA	SAR	TD	TD	CM	TD
Mid-range 1,3-Butadiene 45% 1,3-butadiene, 20% butanes, 30% butenes	v	v	v	v	RA	RA	NA	NA	NA	SAR	TD	TD	CM	TD
Low 1,3-Butadiene[2]	T	T	T	T	T	T	NA	NA	NA	SAR	TD	TD	CM	TD

v Adequate existing data available
1 These data are not yet available, but should be addressed as part of the SIDS program
2 The target concentration of 1,3-butadiene is 10%. Actual composition will be determined analytically and provided when testing is complete.
NA Test not applicable due to physical nature of category member

TD Technical discussion proposed
CM Computer Modeling proposed
RA Read Across

T Proposed Testing

SAR Structure Activity Relationship

Appendix I

ETHYLENE PROCESS DESCRIPTION

A. The 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 unsaturated hydrocarbons. 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 products. 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 hydrocarbon products are also formed, including other olefins, diolefins, aromatics, paraffins, and lesser amounts of acetylenes. These other hydrocarbon products include compounds with two or more carbon atoms per molecule, i.e., C2, C3, C4, etc. Propane and propylene are examples of C3 hydrocarbons and benzene, hexene, and cyclohexane are a few examples of the C6 hydrocarbons.

2. Refinery Gas Separation

Ethylene and propylene are also produced by separation of these olefins 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. Products of the Ethylene Process

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 (C2+). The relative amount of each component 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 product is produced when the cracked gas is initially cooled. The ethylene process is a closed process and the products are contained in pressure systems. (See figure 1 for a pictorial representation of the ethylene manufacturing process.)

The final products of the ethylene process include hydrogen, methane (frequently used as fuel), and the high purity products ethylene and propylene. Other products of the ethylene process are typically mixed streams that are isolated by distillation according to boiling point ranges. It is a subset of these mixed streams that make up the constituents of the Crude Butadiene C4 category.

C. The Crude Butadiene C4 Products

1. Crude Butadiene Or Butadiene Concentrate

Butadiene concentrate is the product in the C4 Crude Butadiene Category. The concentrate is separated by distillation from the condensed portion of the cracked gas. Typically, butadiene concentrate is a fairly narrow boiling range mixture and consists predominately of C4 hydrocarbons. The butadiene concentrate may also contain lesser amounts of C3 or lighter hydrocarbons and C5 and heavier hydrocarbons, because the separation technology is not perfect. The 1,3-butadiene content of this product is typically 40% to 60%, but has been reported to range from 10% to about 80% (table 2). Crude butadiene is sometimes produced in "on purpose" butadiene units using, for example, an oxydehydrogenation process.

2. High Butadiene-Content Heavy Ends From The Butadiene Plant

Several different technologies are used to separate 1,3-butadiene from C4 butadiene concentrate produced by the ethylene process. All of these processes use a solvent for the separation.

In one technology, the C4 butadiene concentrate is fed to an extractive distillation (ED) column and a C4 mixture referred to as “raffinate” (i.e., C4 olefins and paraffins) is separated from the top of the distillate column. The bottom from the ED column consists of the solvent, rich in 1,3-butadiene, and small amounts of other C4s. The rich solvent is fed to the solvent stripper where the 1,3-butadiene and other C4s are taken overhead. The stripped, lean solvent is transferred from the bottom of the stripper back to the ED tower. The overhead of the

stripper is condensed and fed to the rerun tower (or postfractionator) where high purity 1,3-butadiene is produced as the overhead. Bottoms of the rerun tower consist of the higher boiling components of the butadiene concentrate (e.g., 1,2-butadiene). The 1,3-butadiene content of the heavy ends from the butadiene plant covered by this test plan ranges from 13% to 92% (table 2).

3. Full-Range Butadiene Concentrate

Butadiene concentrate sometimes consists of the entire C3+ or C4+ portion of the cracked gas stream (full-range butadiene concentrate). In this case, the carbon number distribution is between C3 and C12 or even higher. Normally the C4+ full-range butadiene concentrate is split by distillation into two streams, a butadiene concentrate stream, described above, and pyrolysis gasoline stream. The C3+ stream is separated into these two streams plus a C3 stream. The C3 stream and pyrolysis gasoline will be covered by separate test categories sponsored by the CMA Olefins Panel. There are only two known examples where these broad-range streams have been reported to have been isolated. In both cases, it was a result of a shutdown of process equipment. The C4+ stream was site limited and the C3+ was not. The 1,3-butadiene content of full range butadiene concentrate has been reported to range from 12% to 42% (table 2).

4. 1,3-Butadiene

High purity 1,3-butadiene (99.5%+) is produced by separation from the C4 butadiene concentrate (or crude butadiene) produced by the ethylene process. This separation is accomplished by using a solvent process, either extraction or more typically extractive distillation. “On purpose” units also produce a small percentage of the commercially available 1,3 butadiene by dehydrogenation and subsequent separation.

Figure 1. Flowsheet for Crude Butadiene C4 Test Group

Note: In addition to Crude Butadiene C4 products & streams, additional HPV products & streams associated with these units are show below for clarity.

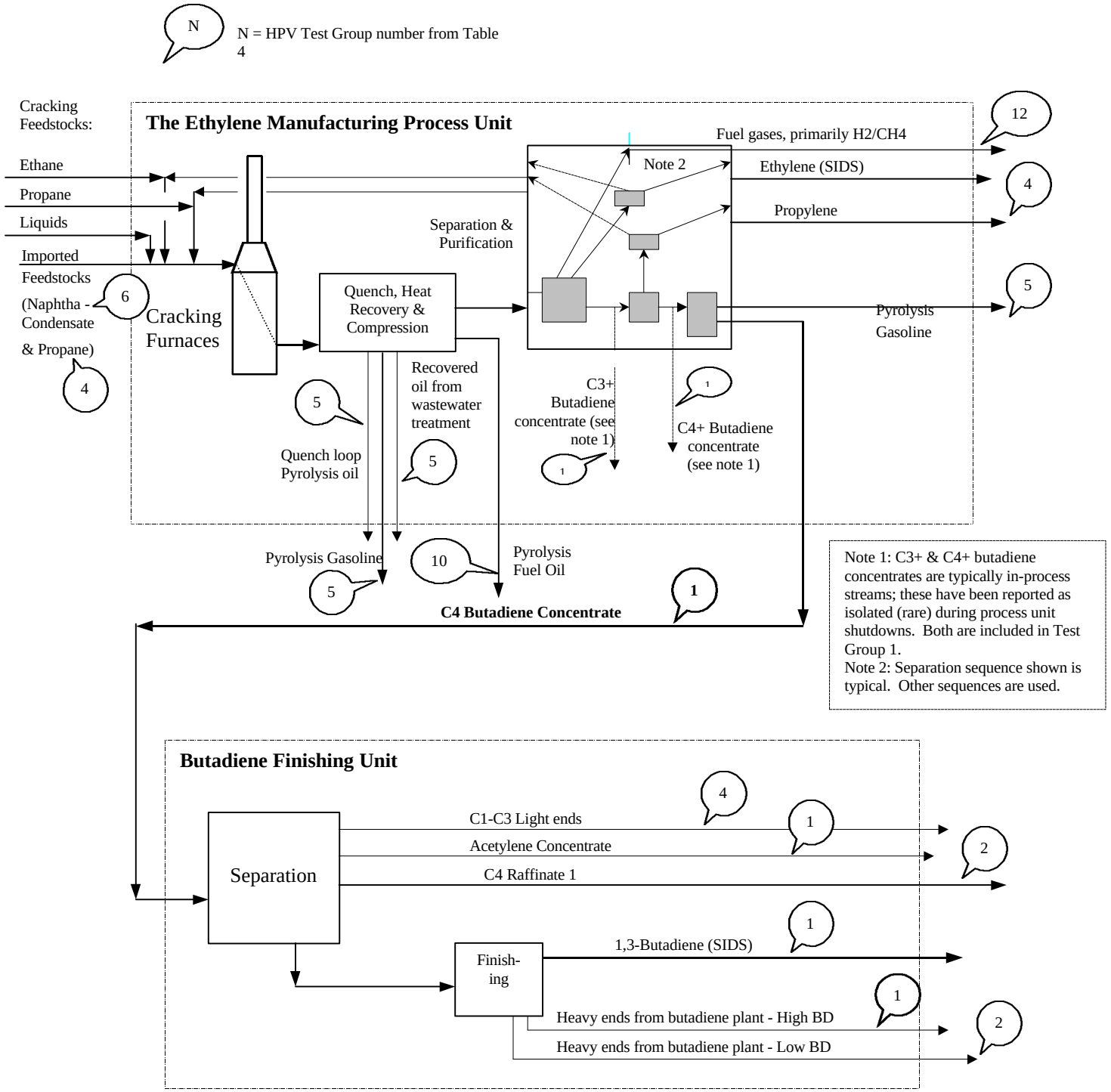

Table 4. CMA Olefins Panel Sponsored Test Categories

Category Number	Category Description
1	Crude Butadiene C4
2	Low Butadiene C4
3	C5 Non-Cyclics
4	Propylene Streams (C3)
5	High Benzene Naphthas (C6-C12, predominantly C6)
6	Low Benzene Naphthas (C7-C12)
7	Resin Oil - High Dicyclopentadiene
8	Resin Oil - Low Dicyclopentadiene
9	Resin Oil - Dicyclopentadiene Concentrate and Crude Dicyclopentadiene
10	Fuel Oils (C8+)
12	Fuel Gases

September 13, 2000

Betty Moran
Manager, Olefins Panel
American Chemistry Council
1300 Wilson Blvd.
Arlington, VA 22209

Dear Ms. Moran:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the Crude Butadiene C4 category, submitted May 9, 2000. I commend the ACC Olefins Panel for their commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will adequately characterize each SIDS endpoint. On its Chemical RTK HPV Challenge Program website EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the attached Comments on the Chemical RTK web site within the next few days. As noted in the comments, we ask that the Panel advise the Agency, within 60 days of the posting on the Chemical RTK website, how it intends to pursue its activities on these chemicals. Please respond either by email (oppt.ncic@epa.gov, hpv.crtk@epa.gov, or chem.rtk@epa.gov)or by regular mail to:

Carol Browner, Administrator
US Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116
Attention: Chemical Right-to-Know Program

EPA will post your response on the Chemical RTK website.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-260-3470. Submit general questions about the HPV Challenge Program through the Chemical RTK web site comment button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@.epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
C. Auer
N. Patel
A. Abramson

EPA Comments on Chemical RTK Challenge Submission: Crude Butadiene C4s

SUMMARY OF EPA COMMENTS

The sponsor, the CMA (now ACC) Olefins Panel's HPV Implementation Task Group, submitted Robust Summaries to EPA and a Test Plan and Category Justification dated May 9, 2000. EPA posted the submission on the ChemRTK website on May 19, 2000. The proposed information-gathering plan is for 1,3-Butadiene (CAS No. 106-99-0) and eleven CAS-numbered petroleum process streams containing 1,3-butadiene, all considered by the sponsor to constitute a Crude Butadienes category.

EPA has reviewed this submission and has reached the following conclusions:

1. The submission comprised an acceptable category submission and test plan overall. While the descriptive material has some confusing aspects and inconsistencies, the sponsor's intentions are adequately clear.

2. As a rule, measured physicochemical property data should be provided, both to characterize a substance and to provide inputs to transport/distribution models; these should be available from published sources on the generally well-known butadiene mixture components. The Test Plan for physicochemical properties suggests that all data on these properties will be derived from EPIWIN calculations.

3. EPA concurs that these gaseous substances are not amenable to environmental fate testing under the Challenge Program. The sponsor plans to use the EQC Level I steady state model to develop distribution data on individual mixture components. However, recent experience in the use of distribution models has caused EPA to conclude that the EQC Level III model gives better results.

4. EPA is concerned that the sponsor's approach to characterizing "full-range butadiene concentrate" may be inadequate. Although the plan to use data from butadiene, benzene, and other related HPV Challenge categories to address the toxicity of this substance may be sufficient, details are sparse, and EPA has not yet received the Panel's test plans for related categories. Thus not all the information necessary to evaluate this part of the test plan may be available. EPA reserves judgement on this point until test plans are available for all the streams containing aromatics.

5. EPA believes further acute inhalation toxicity testing will not be informative for the Challenge Program, as existing limit-test data on 1,3-butadiene and the midrange test substance show no lethality. If the sponsor needs this type of testing for other purposes, EPA suggests that a limit test be performed.

6. The 10% butadiene test substance should be properly characterized. Care should be taken to ensure that the 10% butadiene test substance has a similar component profile to the mid-range butadiene test substance in order to assure comparability of results. The 10% butadiene test substance should be fully characterized by listing all components in the stream and their percentages.

7. The OECD SIDS program's reproductive toxicity analysis for 1,3-butadiene is not yet complete. Resolution of this endpoint will have an impact on this category proposal. EPA believes it is appropriate to understand the outcome of the OECD SIDS process for 1,3-butadiene to better inform the reproductive hazard evaluation of 100% butadiene and the proposal to test 10% butadiene.

8. EPA is concerned that the reproductive/developmental toxicity results for 1,3-butadiene and the 10% butadiene test substance be reasonably comparable. Interpolating the reproductive and developmental toxicity results to the mid-range butadiene stream requires a comparison between the 100% butadiene and the 10% butadiene mixture. There needs to be a reasonable basis for comparison, which may mean comparable protocols and/or test species and a similar mixture component profile as discussed under #6 and #7 above.

9. The mouse appears to be the preferred species for health effects testing On the basis of repeat-dose, mutagenicity and developmental toxicity studies, mice appear more sensitive than rats to 1,3-butadiene. The sponsor has not indicated a species preference for the proposed testing. EPA suggests that the sponsor consider conducting the remaining *in vivo* health effects studies in mice. It would also be helpful to know what test protocols will be used.

10. A few robust study summaries were considered inadequate. Details appear in the text under "Specific Comments on Robust Summaries."

11. As with all category proposals, the outcome of the proposed testing may change the approach to the category as originally proposed.

EPA is requesting that the Sponsor advise the Agency within 60 days how it intends to pursue activities on the proposed test plan.

EPA COMMENTS ON THE CRUDE BUTADIENE C4 CHALLENGE SUBMISSION

EPA's comments are organized as follows: General; Category Description; Category Justification; Test Plan; Specific Comments on Robust Summaries.

General

The sponsor supplied a complete package. The test plan was thorough and included a flow diagram that showed the complex petroleum refining processes and how the proposed category of butadiene streams fits into the larger picture, although the text was not perfectly matched to the diagram. There was some inconsistency in nomenclature in the text. The robust summaries were reasonably well organized

Category Description

General Clarity

The description was sometimes confusing and difficult to assimilate. The process diagram is helpful but would be more so with additional labeling to reflect the description in the text.

Some examples of confusing usage:

> There is no process stream in the Flowsheet that is identified as the "full-range butadiene concentrate" referred to frequently in the text.
>
> "Crude butadiene" is defined in section II. A as "[t]hose mixtures containing 10 to 92% 1,3-butadiene...", but in the title to section C.1 of Appendix I, "crude butadiene" appears to be synonymous with "butadiene concentrate", which contains 10-80% 1,3-butadiene.
>
> Again in Appendix I, it is unclear if "C4 butadiene concentrate" is different from "butadiene concentrate" mentioned in Sections C.1 and C.2.

Despite these shortcomings, EPA agrees that the important point that emerges is the existence of different streams containing a range of possible 1,3-butadiene concentrations.

The category is simply 1,3-butadiene plus the three generic streams (full-range butadiene concentrate, butadiene concentrate, and high butadiene heavy ends) associated with the ethylene production process. Some difficulty arises with the fact that, except for 1,3-butadiene, any of the nominal CAS-numbered category members may be associated with any of the three streams, according to the sponsor. However, EPA acknowledges that petroleum refining processes and products, as well as the chemical composition of such complex mixtures, do not lend themselves to a simple, straightforward assignment to a "traditional" category in the U.S. HPV Challenge Program.

Category Justification

The submission presents a case for considering Crude Butadiene C4 substances as a category. EPA believes the presentation adequately supports this proposal.

This is the first example of a submission to the Challenge Program that is based on a) process streams, and b) the presence of a single well-characterized component of all the streams, 1,3-butadiene, that the submitter proposes will determine the toxicity of all the mixtures listed in the proposal. The submitter also plans to review data on other mixture components that already exist or are in development under

other test plans under the HPV Challenge or other programs "to assist...in determining whether butadiene is the most biologically active component of the Crude Butadiene C4 streams."

EPA believes that, for these mixtures, estimating toxicity on the basis of their 1,3-butadiene content is a reasonable proposal for the health effects portion of the SIDS.

However, EPA is concerned that the sponsor's approach to characterizing "full-range butadiene concentrate" may be inadequate. Although the plan to use data from butadiene, benzene and other higher-than C_4 constituents, and other related HPV Challenge categories to address the toxicity of this substance may be sufficient, it lacks details and sponsors have not yet submitted test plans for related categories. Thus reviewers may not have all the information necessary to evaluate this part of the test plan.

Test Plan

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient). The sponsor plans to develop data on individual mixture components, using EPIWIN, and provide ranges of values for the different streams. However, EPA emphasizes that measured data shoiuld be provided for this purpose. With chemicals such as these mixture components that are well characterized or are being characterized in OECD SIDS and other programs, acceptable literature data may be available for many physicochemical endpoints and should be included wherever possible. (Generally, the log P value can be calculated for chemical classes that have been validated for the calculation.)

Fate (photodegradation, stability in water, biodegradation, and transport/distribution). EPA concurs that these substances are not amenable to environmental fate testing. The sponsor plans to develop distribution data on individual mixture components, using available models. The test plan cites the EQC Level I steady state model as one accepted by EPA in its guidance for the Challenge program. This attribution is correct. However, recent experience in the use of distribution models has caused EPA to conclude that the EQC Level III model gives better results.

As stated above under Chemistry, as a rule measured values rather than calculated physicochemical values should be used as inputs for the models.

Additionally, in situations of this kind, reviewers would find it useful to know which components of the streams sponsors intend to model.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity). EPA agrees with the proposed plan to conduct all the health effects studies on a low-end (e.g., 10% butadiene) mixture. However, EPA does not agree that an acute inhalation toxicity study is informative for the purposes of the U.S. HPV Challenge Program (see item 4 below).

EPA does have some concerns about details provided in the proposal:

(1) EPA assumes that the 10% butadiene test substance will come from either the "crude butadiene/butadiene concentrate" or "heavy ends" streams as identified in Table 2 of the Test Plan. Whichever is used, it does not correlate closely to the third stream ("full-range butadiene concentrate") which is the only stream with components higher than C4. More importantly, the two "C4 streams" appear to have different components (and amounts of each component). Care should be taken to ensure that the 10% butadiene test substance contains the same non-butadiene components as the mid-range butadiene test substance in order to attribute any effect (or lack thereof) to 1,3-butadiene. This requires that the 10% butadiene test substance be fully characterized by listing all components in the stream with their percentages.

(2) Assuming that a 10% butadiene test substance is used in a combined test protocol as proposed, in order to interpolate the reproductive/developmental toxicity results to the mid-range butadiene stream a comparison between the 100% butadiene and the 10% butadiene stream needs to be made. There needs to be a reasonable basis for comparison which may mean the need for comparable protocols (see item 3 below)and/or test species (see item 5 below).

(3) The reproductive toxicity of 1,3-butadiene has not yet been resolved in the OECD SIDS program. Resolution of this issue will affect this category proposal. EPA will reserve comment on this endpoint for 1,3-butadiene until the sponsor develops this argument more fully by incorporating the OECD SIDS assessment findings. EPA believes whatever test protocol(s) are identified/used will affect this category analysis as outlined in item #2 above.

(4) For the purposes of the U.S. Challenge Program, EPA believes that an acute inhalation toxicity study may not be informative. Available test results show that pure butadiene and the mid-range butadiene did not cause lethality at or above the limit of 5 mg/L for such tests and differences in proportions of constituents between the midrange and 10% butadiene mixtures are unlikely to result in significant acute toxicity of the latter. However, if the sponsor needs this type of testing for other purposes, EPA suggests a limit test.

(5) On the basis of repeat-dose, mutagenicity and developmental toxicity studies presented in the Test Plan, as well as many other examples in the literature, it appears that mice are more sensitive than rats to 1,3-butadiene. EPA suggests that the sponsor consider conducting the remaining *in vivo* health effects studies in mice. With test plans of this kind it would be useful to know what test protocols will be used.

Ecological Effects. Because these substances are gases that are rapidly lost from water, EPA accepts the sponsor's proposal to calculate toxicity data for selected mixture components, using ECOSAR or an equivalent aquatic toxicity estimation program. (Gases having properties different than those in this category could be found to need testing; methods are available to address such situations.) Note that when using ECOSAR to predict toxicity values, the CLOGP version of the octanol/water partition coefficient (Log Kow) should be used instead of the Log Kow that EPIWIN automatically enters. This is because ECOSAR values were developed using CLOGP.

Specific Comments on Robust Summaries

The only robust summaries submitted described health effects studies. Seventeen studies were submitted. EPA evaluated each acute, repeat dose, and genotoxicity robust summary and determined that all but one were adequate summaries for the purposes of the U.S. HPV Challenge Program. The robust summary for irritation screening in rabbits with CAS # 68955-28-2, while not among the required SIDS endpoints, was reviewed for its relevance to the test plan.

The *in vivo* mouse dominant lethal assay summary was considered inadequate because the basis for dose selection is not stated. Since there were both positive and negative results (depending upon time point of evaluation), this is considered a critical omission.

Acute Toxicity. Two robust summaries describing acute inhalation toxicity studies, one with CAS # 68955-28-2 (45% butadiene, 20% butanes, and 30% butenes) and one with CAS # 106-99-0 (1,3-butadiene) were reviewed.

The study performed with the 45% butadiene content substance reported a 4-hour LC50 of > 5300 mg/m^3 (5.3 mg/L) in rats (the limit test for inhalation studies is 5 mg/L, or 5000 mg/m^3). Therefore the test mixture used can be considered a low acute inhalation toxicity hazard. (NOTE: The summary lists OECD Test Guideline (TG) 402 as the study protocol but it is likely that OECD TG 403 was used; 402 is for dermal studies).

The 100% butadiene study was not run under GLP conditions. It describes a study in rats and mice showing a 4-hour LC50 of 285 mg/L (much higher than 5 mg/L limit test) in rats and a 2-hour LC50 of 270 mg/L in mice. No experimental details were provided and data quality cannot be determined; thus the study summary is inadequate.

Taken together, these studies show that these gases present a low acute inhalation toxicity hazard and there appears to be no significant difference in response. EPA believes that the difference in proportions of constituents between the midrange and 10% butadiene mixtures is unlikely to result in significant acute toxicity of the latter.

Repeat Dose Toxicity. Three robust summaries describing repeat dose studies were reviewed, two with CAS # 106-99-0 and one with CAS # 68955-28-2.

A subchronic inhalation study in B6C3F1 mice was conducted by the National Toxicology Program. The purpose of the study was to establish doses for a 2-year bioassay. Doses of 0, 625, 1250, 2500, 5000, or 8000 ppm (0,1250, 2500,10000, 16000 mg/m^3) 1,3-butadiene were administered to mice (10/sex/dose) for 6 hours/d, 5 days/wk, for 14 weeks. Mortality was observed at the two higher doses. A NOAEL was established at 1250 ppm based on reduced body weight gains. Histopathological examinations were performed on controls and high dose animals and no effects were observed.

The second 1.3-butadiene summary describes a subchronic inhalation study in which Sprague-Dawley rats (40/sex/dose) were given doses of 0, 1000, 2000, 4000, or 8000 ppm 1,3-butadiene for 6 hours/d, 5 days/wk, for 13 weeks. There were no mortalities. A NOAEL was established at > 8000 ppm and the only exposure-related findings were increased salivation (females after 8 weeks' exposure) and decreased grooming (males after 10 weeks' exposure). Histopathological examinations were performed on controls and high dose animals and no effects were observed.

In the third study, Fisher 344 rats (5/sex/dose) were exposed to the CAS # 68955-28-2 via inhalation 6 hours/d, for nine days over a 12-day period at doses of 0, 1110, and 11,140 ppm). There were no significant effects in the rats over the course of the study. The only effect observed was nasal discharge in some rats in both treated groups, with a greater incidence in the high dose group. Thus, the NOAEL for this study was >11,140 ppm.

Taken together, these studies demonstrate the species differences in response (mortality and reduced body weight gain) to 1,3-butadiene exposure (mice being more susceptible than rats). The two rat studies suggest that 100% butadiene and a mid-range butadiene (45%) produce similar results; however, the test protocols used were quite different (13 weeks of exposure versus 12 days). There are no comparison data for mice, which were tested only with 1,3-butadiene itself.

Genotoxicity Studies. Seven robust summaries were reviewed, for genotoxicity and related effects (cell transformation) and all were properly summarized.

a) 1,3-Butadiene (CAS# 106-99-0)

The *Salmonella typhimurium*/mammalian microsomal (Ames) assay showed 1,3-butadiene to be a weak mutagen with activation (positive in one of four strains tested with uninduced rat and mouse liver enzymes and induced rat liver enzymes).

The *in vivo* micronucleus assay in male rats and female mice by inhalation showed a positive response by inducing micronuclei in the peripheral blood and bone marrow erythrocytes in mice at all dose levels (50, 200, or 500 ppm via inhalation 6 hours/day for 5 days), whereas there was a negative response in rats given the same treatment.

b) Butadiene concentrate (CAS# 68955-28-2) - (Gases (petroleum) light steam-cracked, butadiene conc.) Approximately 45% 1,3-butadiene, 20% butanes and 30% butenes.

The *Salmonella typhimurium*/mammalian microsomal (Ames) assay was negative in all strains tested with and without metabolic (rat only) activation.

The L5178Y $TK^{+/-}$ mouse lymphoma gene mutation assay *in vitro* assay showed a positive response without metabolic activation and a negative response with metabolic activation (rat liver enzyme preparations were used for activation).

The *in vivo* micronucleus assay in male and female mice by inhalation showed a positive response by inducing micronuclei in the bone marrow erythrocytes in mice at all dose levels (10, 780; 20, 670; or 35, 340 ppm via inhalation 2 hours/day for 2 days).

The unscheduled DNA synthesis (UDS) assay in rat hepatocytes *in vitro* showed a weak positive response.

The cell transformation assay in BALB/3T3 cells *in vitro* showed a negative response.

Taken together, the data presented by the sponsor show that 1,3-butadiene appears to affect the chromosome and that mice appear to be more sensitive for this endpoint than rats. Comparing the results (mouse only) of the 45% butadiene micronucleus assay with the 100% butadiene micronucleus assay suggests that the butadiene-based category proposal has merit for this endpoint.

Reproductive Toxicity Studies. The Test Plan indicates that adequate data are not yet available for 1,3-butadiene, but they should be addressed in the OECD SIDS program. However, data are presented from two studies (spermhead morphology and dominant-lethal studies, both in mice) on 1,3-butadiene that are informative in addressing reproductive toxicity. In both cases, the robust summaries are considered inadequate because the basis for dose selection is not provided. EPA believes this inadequacy is not

critical for the spermhead morphology study because the results were positive.

> A sperm morphology assay in which 20 CD-1 male mice were exposed to 0, 200, 1000, 5000 ppm 1,3-butadiene via inhalation 6 hours/day for 5 days showed a positive response (slight but dose-related increase in abnormal sperm heads with dose).
>
> The *in vivo* mouse dominant lethal assay in males exposed by inhalation does not indicate the basis for the dose selection. Since the results were both positive and negative (depending upon the time point of evaluation), this is a critical omission.

EPA believes it is appropriate to understand the outcome of the OECD SIDS process for 1,3-butadiene to better inform the reproductive hazard evaluation of 100% butadiene and the proposal to test 10% butadiene.

Developmental Toxicity Studies. The robust summaries of the two inhalation developmental toxicity studies (in rats and mice, both with 100% 1,3-butadiene) are adequate. However, EPA has the following comments:

> The LOAEL and the basis for that effect level should be specifically cited in the Results section for the robust summaries for both developmental toxicity studies.
>
> In the robust summary for the mouse study:
>
> > (1) signs of developmental toxicity in mice (decreases in fetal weights, increases in fetal variations) were reported at concentrations of 200 and 1000 ppm. The decreases in fetal weights were reported as being significantly reduced while the increases in fetal variations were reported as being 'increased'. There needs to be some mention of whether or not this increase was statistically significant; and
> >
> > (2) in the Results section, fetal weights were reported as being reduced in both males and females, while in the Conclusions section, this endpoint was reported as a "slight statistically significant decrease in male fetal weight". This needs to be clarified as to whether the reduction in female fetal weight was significant.

Signs of developmental toxicity in mice (significant decreases in fetal body weights and increases in fetal variations) were observed at 200 ppm and 1000 ppm. No signs of developmental toxicity were observed in rats at concentrations as high as 1000 ppm. As in the case of repeat-dose and mutagenicity studies, it appears that mice are more sensitive than rats to 1,3-butadiene.

Followup Activity

EPA requests that the Sponsor advise the Agency within 60 days how it intends to pursue activities on the proposed test plan.

PETA
PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS
501 FRONT STREET
NORFOLK, VA 23510
TEL 757-622-PETA
FAX 757-622-0457

September 18, 2000

The Honorable Carol Browner
Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

Subject: Comments on "Test Plan for Crude Butadiene C4 Category"

Dear Administrator Browner:

The following comments on the Test Plan for Crude Butadiene are submitted on behalf of People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, Physicians Committee for Responsible Medicine, and Earth Island Institute. These animal protection and environmental organizations have a combined membership of more than nine million Americans concerned with the suffering of animals used in laboratories.

Again, we reiterate the request made in our August 21 letter to you that the EPA respond specifically to our concerns and detail the manner in which the agency intends to ensure that the spirit and the letter of its October 14, 1999, letter to HPV participants are followed. The agency's comments on the first two test plans appear to revert to a "check-the-box" exercise in testing for testing's sake that was specifically proscribed in that October letter. To date, we have not received any response from the EPA on this important matter.

General Comments

The test plan for crude butadiene, submitted by the Chemical Manufacturers Association (CMA) provides a case study in the wide-ranging number of technical and policy issues raised by the high production volume (HPV) chemical-testing program. These issues include:

- The need for coordination among different industries in developing categories of substances in the HPV program.
- The importance of documenting specific tests prior to test plan implementation.
- Compliance with the spirit and letter of guidance provided by EPA to HPV program participants in the form of the October 14, 1999, letter.
- Conducting animal testing for endpoints that are physically, environmentally, or toxicologically irrelevant.

- Testing mixed composition industrial streams when they are mixtures of compounds whose toxicity is already well understood.
- The general problem of high interspecies variability in toxicological testing resulting in data providing minimal insight into potential human toxicity.
- Conducting more animal tests on well-characterized compounds with an extensive human epidemiological and toxicological database.

Comments on the Crude Butadiene C4 Category

The CMA Olefins Panel has addressed some of the key issues outlined above. However, this plan also demonstrates the obvious pitfalls of crude, check-the-box toxicological testing, and neglects specific guidance developed for the HPV program by EPA regarding animal testing.

The CMA has done an excellent job of grouping twelve different industrial streams with separate CAS numbers into a single category, recognizing that 1,3 butadiene is the primary bioactive agent in all these mixtures. In addition, in evaluating the potential toxicity of many constituents in these streams, CMA is anticipating coordinating its efforts with other compound groups being developed by CMA and the American Petroleum Institute (API). In reviewing previous test plans,[1] we have expressed concern that this sort of coordination had not occurred. We hope that future test plans will be developed with the cooperation among separate industry consortia that is the case here. Our hope is that this coordination will reduce the number of animals killed in this testing program and we anticipate following the process closely.

One major problem with this test plan is that CMA has provided only a sparse description of the specific test methods it plans to use in conducting "one test battery for all SIDS human health endpoints." As a matter of fact, the test plan's executive summary makes no mention of the tests that will be conducted. The plan fails to specifically outline the applicable test methods being proposed, with complete references. Through a review of OECD documents and the robust summaries, we have been able to gain some insight into the specific testing proposed by CMA but we are unable to obtain a complete understanding of all the proposed testing. At a minimum, CMA should identify the exact method it is planning to use for each human health endpoint test, and provide information on whether the tests are *in vivo* or *in vitro*, the species to be used, the exposure method, and the exposure time. For example, the exact method to be used to determine acute toxicity should be clearly stated (e.g., LD-50, fixed dose, up-and-down, acute toxic class).

Further, the proposed test plan ignores the guidance provided in the EPA letter to HPV chemical testing participants dated October 14, 1999. This letter was the result of a negotiated agreement in which the CMA played a key role. This letter states in part:

[1] PETA letter to Carol Browner dated August 21, 2000 (not posted on EPA website as of 9-18-2000).

"1. In analyzing the adequacy of existing data, participants shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach. Participants may conclude that there is significant data, given the totality of what is known about a chemical, including human experience, that certain endpoints need not be tested." And,

"8. As with all chemicals, before generating new information, participants should further consider whether any additional information obtained would be useful or relevant."

1,3 butadiene toxicity is well understood at both an empirical and biochemical level. These data are well supported by extensive epidemiological data based on worker exposure. Further, the toxicity of other compounds in the crude butadiene streams are well-characterized and are usually much less bioactive than 1,3 butadiene. Despite these facts, the CMA is proposing an extensive set of animal tests to evaluate potential health effects.

As clearly stated in the test plan (Table 2), crude butadiene streams consist primarily of well-characterized simple four carbon compounds. Existing data shows that mid-range butadiene streams are less toxic than one would calculate based on 1,3 butadiene content alone. Yet the CMA is still proposing to conduct a series of animal tests on a stream with an even lower 1,3 butadiene content. This testing is wholly inappropriate and unnecessary.

The additional testing on the low butadiene stream also will provide little useful data for use in regulation, industrial hygiene, or emergency response. The 1,3 butadiene concentration in air is already regulated at very low levels in industrial settings, with a permissible exposure level (PEL) of less than 1 ppm weighted over an 8 hour period. The PEL is based on epidemiological and toxicological analyses of workers and previous animal studies[2]. The crude screening-level tests proposed in this test plan will provide no insight into the regulation of butadiene in the workplace, especially given the extensive toxicological work already being conducted on the metabolism of butadiene in humans[3,4,5]. Rather, it is the issues of human metabolism of 1,3 butadiene and the resulting cancer-causing mechanism that need further study and evaluation.

Further evidence of the irrelevance of the proposed tests is the acute inhalation toxicity testing for the crude butadiene stream. Existing animal data shows that acute toxicity for

[2] Material Safety Data Sheet for 1,3 Butadiene. Chemical Safety Associates, Inc. January 23, 1998.
[3] M. G. Bird. International Symposium on the Evaluation of Health Risks of Butadiene and Isoprene: General Introduction. Toxicology 113:2-4
[4] Sathiakumar N, Delzell E, Hovinga M, et al.; Mortality from cancer and other causes of death among synthetic rubber worker. Occup Environ. Med. 55(4) 230-5
[5] Kohn MC, Melnick RL: .Species differences in the production and clearance of 1,3-butadiene metabolites: a mechanistic model indicates predominantly physiological, not biochemical, control. Carcinogenesis, 1993 Apr;14 (4):619-28

1,3 butadiene occurs at levels between 10% and 13% in air[6]. In general, the other four-carbon compounds in crude butadiene streams also begin to show acute toxicity at similar to slightly higher levels as butadiene (up to 25%)[7]. At these hydrocarbon levels, a large portion of toxicity is simply due to oxygen displacement and asphyxiation. To put these air concentrations in context, 1,3 butadiene is explosive when it is present in concentrations between 2% and 12% in air (it is not explosive above 12% due to reduced oxygen levels). The explosive ranges of other common constituents of crude butadiene streams are between 1.6% and 10%. It is obvious that killing animals to show that they are asphyxiated by a combination of low levels of oxygen and explosive levels of hydrocarbons is not a productive use of CMA's resources. It is also a cruel and pointless waste of animal lives and clearly violates the principles set forth in points no. 1 and 8 of EPA's October 14, 1999, letter to HPV participants.

Further, the EPA's October 14, 1999, letter placed a two-year moratorium on the testing of individual chemicals in order to allow for non-animal test replacements for some SIDS endpoints, specifically acute toxicity testing. Animal protection organizations were assured by the CMA, prior to that agreement, that category testing would limit the number of animals killed and would consolidate information so that acute toxicity testing would rarely, if ever, be proposed for chemicals grouped into categories. We are extremely disturbed that the CMA has not seen fit to abide by the letter or spirit of that agreement, especially in the face of clear existing toxicity data that could easily substitute for more rote "check-the-box" animal testing.

With regard to the carcinogenic and reproductive effects of butadiene, the results of animal testing demonstrate the extremely limited use of animal data in predicting potential effects in humans. Carcinogenic effects in mice have been observed at levels as low as 6.25 ppm butadiene, while some rat studies have shown no carcinogenic effects at levels as high as 8000 ppm butadiene[8]. The differences in response are attributed to significantly different biochemical mechanisms of butadiene metabolism in these closely related species. The variability in the oncological data in rats and mice illustrates the problems associated with applying toxicological data from one species to another even closely related species. The problem is exacerbated when extrapolating from rodents to humans and is best summarized by Cagen *et al.*[8] (emphasis added):

> "Because of the marked species differences in the carcinogenic response to butadiene, estimates of risk vary over **nine orders of magnitude** going from the most sensitive target organ in female mice to less sensitive male rats. An important tool in determining which estimate is most relevant for extrapolation to humans is to ascertain consistency with human experience. Estimated workplace cancer risks which are based on the

[6] Material Safety Data Sheet for 1,3 Butadiene. Prepared by Chemical Safety Associates, Inc. for Air Products Incorporated. January 23, 1998.
[7] Material Safety Data Sheets for n-Butane, Isobutane, 1-Butene, cis-2 Butene, trans-2 Butene, and Isobutylene. Prepared by Chemical Safety Associates for Air Products Incorporated. All updated in 1998.
[8] Cagen SZ, MacDonald RLM, Van Gelder G; Review of risk assessments on 1,3-butadiene (1985-1991). Toxicology 113, 215-220

> assumption that humans are as responsive as the mouse suggest added risks of 200 or more out of 1000 workers (1 in 5) exposed to 2ppm butadiene (assume 40 years of exposure). This estimate is clearly inconsistent with what has been seen and this would not have been missed in epidemiological studies."

Carcinogenicity has been the most extensively studied toxic endpoint and these studies show the dramatic differences in sensitivity to butadiene among different species. Because these differences have been partially explained by well-characterized differences in toxicokinetics, it is not surprising that other endpoints show similar disparities. As one peer-reviewed summary notes: "Because the mouse is particularly sensitive to butadiene in comparison with other laboratory species, and there are important functional and anatomical differences between humans and mice, the NOELs and LOELs identified for butadiene for various reproductive endpoints in mice may not be relevant to human reproductive risk."[9]

Despite these cautions, calls for additional testing in mice and rats persist, even though butadiene has been extensively evaluated for reproductive and developmental toxicity in both rats and mice.[9,10] According to a recent review published in the journal *Toxicology*, the lowest observable effects for developmental toxicity in mice is 200 ppm. It is 1,000 ppm in rats. Reduced testicular weight is seen in mice at 200 ppm and abnormal sperm heads are seen at 1,000 ppm. One apparently infrequently assessed toxicological manifestation, ovarian atrophy, was seen in the same studies that illustrated carcinogenic effects in mice at 6.25 ppm. But the same review notes: "It may be inappropriate to identify the ovary as the target organ for reproductive risk since the ovarian atrophy in mice was identified after completion of the normal reproductive life and after more than 15 months of exposure." Rats exposed to concentrations as high as 8,000 ppm for two years showed no signs of either testicular or ovarian atrophy. Exposure of rats, guinea pigs, and rabbits to concentrations as high as 6,700 ppm for 8 months did not impair fertility.[10]

As with cancer, the dramatic species differences between mice and rats in reproductive and developmental effects cast serious doubt on the reliability of either in predicting effects in humans. At the same time, one parallel that may exist is the likelihood that carcinogenicity is the most sensitive endpoint in rats, mice, and humans. The lowest observed effect level in mice and rats is considerably lower for carcinogenicity than for reproductive and developmental effects (with the exception of the above-mentioned ovarian atrophy, identified during the carcinogenicity studies and unlikely to be of relevance). Most importantly studies of exposed workers have consistently shown increased incidences of cancer.

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[9] Christian MS: Review of reproductive and developmental toxicity of 1,3 butadiene. Toxicology 1996; 113: 137-43.

[10] Morrissey RE, Schwetz BA, Hackett Pl et al.: Overview of reproductive and developmental toxicity studies of 1,3 butadiene in rodents. Environ. Health Perspect. 1990; 86:79-84.

The extensive human epidemiological data for butadiene can be used to understand the potential effects and to develop a basis for implementing appropriate workplace exposure levels. Further study of exposed workers, including retrospective studies of workers, could be used to better characterize potential reproductive and developmental effects.

In identifying the hazards posed by crude butadiene streams, we suggest using the tools of risk assessment applied across the country at state and EPA Superfund sites. At these locations, cumulative risk is estimated as a product of a compound's toxicity, exposure to individuals via relevant pathways, and duration of exposure. Using data on the specific composition of different crude butadiene streams, the relative hazard of the different streams could be estimated based on their composition and existing toxicological and epidemiological data on crude mixtures and pure compounds. Uncertainty in these calculations could be accounted for by inclusion of an appropriate safety factor, as is done in CERCLA sites. In fact, an innovative toxicologist may even be able to accurately account for competitive binding of different C4 compounds, a toxicological mechanism mentioned in the test plan that results in lower butadiene toxicity.

This hazard analysis may actually be useful in industrial hygiene and environmental decision-making, because the relative hazard from each of the different members of the group could be ranked. As a hypothetical example, this analysis could provide important input into corporate "Green Chemistry" programs, where the relative toxicity of different butadiene streams could be a factor in choosing a feedstock for a specific chemical manufacturing process. By focusing efforts on interpreting the abundant existing data instead of conducting more animal testing, it is likely that a better understanding of the toxicity of these different butadiene streams would be developed.

Summary

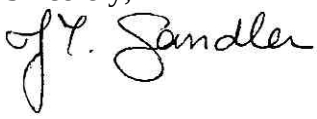
The CMA has developed a costly (both in terms of dollars and animal lives) test plan for butadiene that will provide little information to improve our understanding of the toxicity of crude butadiene streams. Regardless of the outcome of these tests, the handling and emergency response of industrial streams of butadiene will be unchanged, as we already have an extensive understanding of its effects from extensive existing epidemiological data on humans[11,12], and an extensive understanding of its physical and chemical properties. The extreme interspecies variability documented by butadiene exposure in animal tests will render these results insignificant relative to our existing understanding of butadiene toxicity based on epidemiological and biochemical analyses. We therefore recommend that the CMA use the massive amount of already existing toxicological data on compounds in crude butadiene streams as the basis for determining the hazards of the members of this group.

[11] Acquavella JF, Butadiene epidemiology: a summary of results and outstanding issues. Toxicology 113:148-156

[12] Sathiakumar N, Delzell E, Hovinga M, et al.; Mortality from cancer and other causes of death among synthetic rubber worker. Occup Environ Med 55(4) 230-5

I can be reached at (757) 622-7382, ext. 304, or by e-mail at jessicas@peta-online.org. Correspondence should be sent to my attention at the following address: 4800 Baseline Road, #E104-390, Boulder, CO 80305. I look forward to your response on this important issue.

Sincerely,



Jessica T. Sandler, MHS
Federal Agency Liaison

cc: The Honorable Robert C. Smith
The Honorable F. James Sensenbrenner, Jr.
The Honorable Ken Calvert
The Honorable Jerry Costello
Council on Environmental Quality

AR 201-12840

COURTNEY M. PRICE
VICE PRESIDENT
CHEMSTAR

American Chemistry* Council Good Chemistry Maker It Possible

November 9, 2000

Carol Browner, Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22 116
Attention: Chemical Right-to-Know Program

Jessica T. Sandler, MHS
Federal Agency Liaison
People for the Ethical Treatment of Animals
4800 Baseline Road, #E104-390
Boulder, CO 80305

Re: Response to Comments on Test Plan

Dear Ms. Browner and Ms. Sandler:

This letter is submitted by the American Chemistry Council Olefins Panel (Panel) to respond to comments it has received on its test plan and robust summaries for the Crude Butadiene C4 category. Comments were received from the Environmental Protection Agency (EPA) and People for the Ethical Treatment of Animals (PETA).

General Comments and Response

The Panel appreciates EPA's recognition that the Panel supplied a complete package that constituted an acceptable category submission and test plan overall. The Panel also appreciates PETA's recognition that the Panel has formed an appropriate chemical category and is taking appropriate steps to coordinate with the efforts of other industry groups which are addressing related chemical categories.

PETA has raised a number of questions concerning the necessity of the proposed testing. The Panel takes these comments seriously, and agrees with the principles PETA cites from EPA's October 14, 1999 letter, namely that: (1) in analyzing the adequacy of existing data, participants shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach; and (2) before generating new information, participants in the HPV program should consider whether any additional information obtained would be useful or relevant. In this case, however, the Panel believes it has achieved an appropriate balance between identified data gaps and animal welfare concerns.

As the Panel develops test plans for additional chemical categories, the Panel will apply thoughtful, qualitative analyses in lieu of a rote checklist approach, and will make every reasonable effort to avoid unnecessary use of laboratory animals.

Suggestion to Eliminate the Acute Inhalation Test

Both EPA and PETA have recommended against the conduct of an acute inhalation (LC_{50}) test. The Panel agrees with this recommendation and the supporting rationales presented by EPA and PETA, and accordingly will delete this study from the test plan. Moreover, the Panel will not include an acute inhalation study in future test plans for other olefins categories absent some unique justification not present in this case.

Other EPA Comments

EPA has presented several other specific comments. Most of these will be addressed in the Panel's final report for this test plan. We address here one specific comment: EPA's suggestion that the Panel consider conducting the *in vivo* health effects studies in mice, not rats, based on available studies of 1,3-butadiene that show that the mouse is the more sensitive species based on exposure concentrations.

The Panel has considered this comment, and has decided to conduct the OECD Guideline Number 422 study (combined repeated dose/reproductive and developmental effects/neurotoxicity screen) in the rat for several reasons. First, the OECD 422 study was designed for the rat and the standard test protocol specifies the rat as the test species. Second, because the rat is the usual test species for this study, an extensive historical control database exists for the rat. We are not aware of a comparable historical control database for the mouse. Third, for approximately equivalent exposure concentrations of 1,3-butadiene by inhalation, the metabolic profile in rats and mice is remarkably different. Rats form much less of the diepoxide metabolite than mice, and mechanistic studies show that the diepoxide metabolite is obligatory for ovarian atrophy. Fourth, extensive *in vitro* and *in vivo* metabolic studies in mice, rats and human tissues, shows that the metabolic profile of butadiene in humans is more similar to rats than it is to mice. Selection of the mouse as the "most sensitive" species is inappropriate because of its documented unique metabolic status. The Panel believes the rat is the more appropriate test species for the combined repeated dose/reproductive and developmental effects/neurotoxicity screen, in general, and specifically for process streams containing butadiene. The application of the rat as the test species based on available scientific data is expected to provide an assessment of risk more realistically relevant to humans.

In the case of the micronucleus test (OECD Guideline Number 474), where the mouse is the usual test species, the Panel will use the mouse. The Panel believes the mouse is scientifically appropriate because the purpose of the test is to determine the genotoxicity potential of streams containing butadiene, the mouse is the

usual test species for this test, and butadiene does not cause an effect *in vitro* or in a rat micronucleus test. The Panel views the mouse micronucleus test as a mechanistic test, rather than a test to determine potential risk to humans; thus, the use of an overly sensitive test species is not inappropriate.

In summary, the Panel has considered the choice of test species and does plan to use the standard test protocol and standard test species for each mammalian test conducted on Group 1 test streams.

The Panel appreciates the comments it has received from EPA and PETA. Any comments or questions concerning this letter may be directed to Elizabeth J. Moran, Manager of the Olefins Panel, at (301) 924-2006, or via email at Elizabeth_Moran@americanchemistry.com.

Sincerely yours,

Courtney M. Price
Vice President, CHEMSTAR

August 1, 2002

Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency
P. O. Box 1473
Merrifield, VA 22116

RE: Olefins Panel Robust Summaries on HPV Crude Butadiene C4 Category
HPV Registration No. 1101064

Dear Ms. Whitman:

The American Chemistry Council Olefins Panel (Panel) submitted a Test Plan to EPA on May 4, 2000, under the High Production Volume (HPV) Chemical Challenge Program pertaining to the Crude Butadiene C4 Category. With this letter, the Panel submits robust summaries of certain calculated parameters under the test plan. The Panel also provides an update on the status of reporting for this HPV category.

The Test Plan for the Crude Butadiene C4 category included technical discussions to address aquatic toxicity, photodegradation, hydrolysis, and biodegradation and the calculation of fugacity. Physicochemical data would also be calculated as described in the EPA document titled, *The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program.* Robust summaries for this information are listed in attachment and are enclosed.

The Test Plan also proposed using data from other test programs under the OECD SIDS or HPV Challenge Program to complete characterization of the toxicity of the streams in this category. The Panel plans to submit a report on the category after the data to fully characterize the category are available under these programs.

If you have any questions, please contact Dr. Elizabeth Moran, Manager of the Olefins Panel at 301 924 2006 or Elizabeth_Moran@americanchemistry.com.

Sincerely yours,

Courtney M. Price
Vice President, CHEMSTAR

attachments
cc: C. Auer (EPA)
O. Hernandez (EPA)
J. Keith (ACC)

Attachment 1
Robust Summaries for Calculated Parameters
For Olefins Panel Crude Butadiene C4 Category

Calculated Vapor Pressure
Calculated Boiling Point
Calculated Melting Point
Calculated Water Solubility
Calculated Partition Coefficient
Calculated Biodegradation
Calculated Transport/Distribution (Fugacity)
Calculated Hydrolysis (Stability in Water)
Calculated Photodegradation (Direct)
Calculated Photodegradation (Indirect)
Calculated Daphnid Acute Toxicity
Calculated Fish Acute Toxicity
Calculated Alga Toxicity

AR201-13901 B

Calculated Alga Toxicity

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CRUDE BUTADIENE C4 ROBUST SUMMARY

Alga Toxicity

Test Substance*:	Other TS
Method/Guideline*:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type):	Green Alga Toxicity Calculation; EC50
GLP:	Not applicable
Year (study performed):	Not applicable
Species:	Freshwater Green Alga (calculated toxicity values are not species specific)
Analytical Monitoring:	Not applicable
Exposure Period:	96 hours
Statistical Method: (FT - ME)*	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPIWIN computer model (2). KOWWIN also has a database of experimental Kow values (EXPKOW.DB). The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of toxicity data for component chemicals is an estimate of the potential toxicity of category products.

Chemical	Calculated log K_{ow}	Measured* log K_{ow}
Isobutane	2.23	2.76
n-butane	2.31	2.89
isobutylene	2.23	2.34
cis-butene-2	2.09	2.31
trans-butene-2	2.09	2.33
butene-1	2.17	2.40
1,3-butadiene	2.03	1.99

* Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	organic compounds with reliably measured values.. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the alga toxicity range of this category are C4 hydrocarbons that are common across the 12 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 category can be found in the American Chemistry Council, Olefins Panel test plan for this category (3). 1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92. 2. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. 3. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**	Calculated alga toxicity values for 7 chemicals representative of products in the Crude Butadiene C4 Category are as follows: Chemical — Calculated log K_{ow} — Alga Toxicity 96-hr EC50 (mg/L) Isobutane — 2.23 — 18.06 n-butane — 2.31 — 15.35 isobutylene — 2.23 — 17.44 cis-butene-2 — 2.09 — 23.19 trans-butene-2 — 2.09 — 23.19 butene-1 — 2.17 — 19.71 1,3-butadiene — 2.03 — 25.27 Chemical — Measured* log K_{ow} — Alga Toxicity 96-hr EC50 (mg/L) Isobutane — 2.76 — 6.13 n-butane — 2.89 — 4.71 isobutylene — 2.34 — 13.94 cis-butene-2 — 2.31 — 14.81 trans-butene-2 — 2.33 — 14.22

Calculated Alga Toxicity

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	butene-1 2.40 12.33 1,3-butadiene 1.99 27.42 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.
Test Substance: (FT - TS)	106-99-0 1,3-Butadiene 25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked 68513-68-8 Residues (Petroleum), Deethanizer Tower
Conclusion: (FT - CL)	Based on the calculated Kow values, products in this category are expected to have an alga 96-hour EC50 range of 15.35 to 25.27 mg/L. Based on the measured Kow values, products in this category are expected to have an alga 96-hour EC50 range of 4.71 to 27.42 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The toxicity values are calculated.
Reference: (FT - RE)	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "acute toxicity to aquatic plants". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:
RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CRUDE BUTADIENE C4 ROBUST SUMMARY

Biodegradation

Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Inoculum:	Not applicable
Exposure Period:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Not applicable
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Not applicable
Test Substance: (FT - TS)	106-99-0 1,3-Butadiene 25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked 68513-68-8 Residues (Petroleum), Deethanizer Tower

Biodegradation

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

Conclusion: (FT - CL)	**Summary** In the environment, biodegradation will not contribute significantly to the loss of chemicals in products from the Crude Butadiene C4 category (C4 refers to a chemical with 4 carbons). This category includes three process streams: • **C4 Crude Butadiene** • **Butadiene Unit Heavy Ends** • **Full-Range Butadiene Concentrates** Twelve CAS numbers (Table 1) identify products derived from these process streams. The products contain various chemicals composed of carbon and hydrogen (Table 2). As discussed below, products in this category are gaseous. If they are released to the environment, their chemical components will partition primarily to the air where they can degrade rapidly by physicochemical reactions. It is far less likely that products from this category will partition to environmental compartments where they could be degraded by bacteria. **The Crude Butadiene C4 Category** A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. Process streams containing 10 to 92% butadiene are referred to as “crude butadiene.” With the exception of CAS 106-99-0 (which is pure 1,3-butadiene), the CAS numbers or streams in this category (Table 1) consist of complex mixtures of hydrocarbons (Table 2). Most commercial products in this category have a carbon number distribution predominantly between C3 and C5. All of these streams contain significant levels of 1,3-butadiene and olefins, which is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Crude Butadiene C4. The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process). Crude butadiene streams arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the three process streams in this category are:

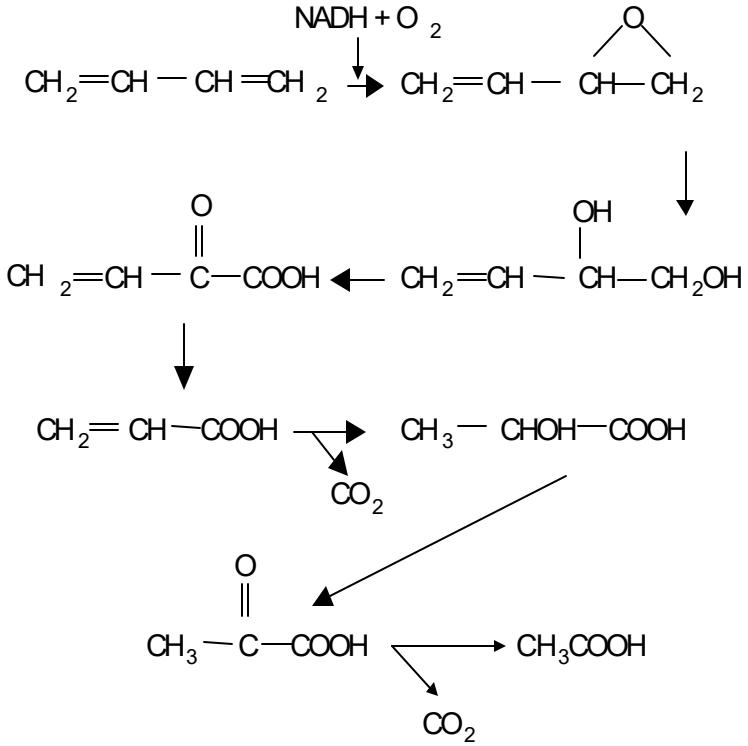
	• **C4 Crude Butadiene** is produced by the distillation of a condensed portion of cracked gas in an ethylene process. C4 Crude Butadiene typically contains 40% to about 60% 1,3-butadiene, but could contain between 10% and 82% butadiene (Table 2). Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. • **Butadiene Unit Heavy Ends** is produced by extractive distillation of cracked gas. The 1,3-butadiene content of this mixed stream ranges from 13% to 92% (Table 2). Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. Only three companies report isolating this stream which is more typically an un-isolated intermediate. • **Full-Range Butadiene Concentrates** is produced from cracked gas after the removal of ethylene or ethylene and propylene. The 1,3-butadiene content of full range butadiene concentrates has been reported to range from 12% to 42% (Table 2). Other chemicals in this mixed stream are those containing three to twelve or more carbons. These streams are intermediates that are not normally isolated in the ethylene process and have been reported as isolated only in infrequent situations. **Biodegradation of Hydrocarbons** Biodegradation is the use of a chemical by microorganisms as a source of energy and carbon. The parent chemical is broken down to simpler, smaller chemicals, which can be converted to inorganic forms such as carbon dioxide, nitrate, sulfate, and water. Products in the Crude Butadiene C4 category are gaseous hydrocarbons, composed predominantly of chemicals with carbon numbers smaller than C5. However, the *Full-Range Butadiene Concentrates* process stream from this category, can contain hydrocarbons greater than C4. These chemicals when isolated individually are not gaseous, but relatively volatile liquids under most environmental conditions. Several hydrocarbons as well as products that are mixtures of hydrocarbons with carbon numbers greater than C4 have been shown to biodegrade. If released to the environment, biodegradation of these chemicals will occur primarily in aquatic and terrestrial habitats. There is sufficient biodegradation data on hydrocarbons in this category that are greater than C4 to show that these chemicals have a potential to biodegrade to a great extent and not persist in the environment (see the *C5 Noncyclics, Low Benzene Naphtha, and High Benzene Naphtha* HPV Chemical Program test plans from the Olefins Panel of the American Chemistry Council, for specific data and a more detailed discussion of the biodegradability of selected hydrocarbons greater than C4.) The larger proportion of chemicals from this category are gaseous. Consequently, their availability to microbial degraders will be significantly limited.

Biodegradation

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

Component chemicals from all three process streams in this category are simple hydrocarbons (Table 2), the majority of which will partition primarily to the air where physical processes will contribute to their degradation [see the atmospheric oxidation potential (AOP) data (as mediated by hydroxyl radical attack) for specific degradation rates of selected chemicals from this category; AOP data were developed for this category under the HPV Chemical Program]. All chemicals from this category that partition to the air are calculated to degrade rapidly due to physical processes and not persist. Because of the partitioning behavior of chemicals in this category, biodegradative processes will be less likely to contribute to their loss from the environment.

Products from the Crude Butadiene C4 category do not lend themselves to being evaluated for biodegradability using standard experimental techniques because of their physical state. However, there is microbial metabolism information for one of the major chemicals, 1,3-butadiene, in this category that demonstrates that it can be biodegraded. Experimental studies to determine a catabolic pathway for 1,3-butadiene as mediated by a *Nocardia* sp. (3) resulted in the following proposed series of reactions:



The intermediary metabolic steps depicted above result in the production of acetic acid, CH3COOH, which can be further metabolized. In addition, 1,3-butadiene has been estimated to have an aerobic aquatic biodegradation half-life ranging from 1 to 4 weeks (2).

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	The potential biodegradability of some of the higher molecular weight components including benzene, toluene, xylene, ethylbenzene, and naphthalene has been summarized and metabolic pathways leading to their biodegradation have been described (4). These compounds have been shown to biodegrade to high extents such that if they were to partition to either a terrestrial or aqueous environment, they would be subject to biodegradative processes that would result in their removal from the environment. In summary, because the C4 and lighter chemical components of this category will partition to the air, physical degradative processes will dominate their fate. Data show that these chemicals are subject to rapid physical degradation. Chemical components of this category that are greater than C4 also have a potential to partition to the air to a great extent, where they will also degrade rapidly in a similar manner. However, they also have a potential to partition to aquatic and terrestrial environments where they are subject to biological processes that can result in their rapid biodegradation. Overall, products from this category and their component chemicals are expected to degrade rapidly in the environment and not persist. **References** 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. Virginia, USA. 2. Howard, P.H., R.S. Boethling, W.F. Jarvis, W.M. Meylan, and E.M. Michalenko. 1991. Handbook of Environmental Degradation Rates. H.T. Printup Ed. Lewis Publishers, Chelsea, MI, USA. 3. Watkinson, R.J. and H.J. Somerville. 1976. The Microbial Utilization of Butadiene. Shell Research Limited, Sittingbourne Research Centre, Kent, UK. 4. van Agteren, M.H., S. Keuning, and D.B. Janssen. 1998. Handbook on Biodegradation and Biological Treatment of Hazardous Organic Compounds. Kluwer Academic Publishers. Boston, CT, USA.
Reliability: (FT - RL)	Not applicable
Reference: (FT - RE)	American Chemistry Council, Olefins Panel. 2002. Hydrolysis: Crude Butadiene C4 Category. Rosslyn, VA, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "biodegradation". Selecting this option refers the reader to information in the "freetext" field for "test substance".

Biodegradation

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

FT - Freetext
IUCLID fields include:
RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CRUDE BUTADIENE C4 ROBUST SUMMARY

Boiling Point

Test Substance*:	Other TS
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Pressure:	760 mm Hg
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Boiling Point estimations performed by MPBPWIN are based on the calculation method of S. Stein and R. Brown in "Estimation of Normal Boiling Points from Group Contributions". 1994. J. Chem. Inf. Comput. Sci. **34**: 581-587.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated BP (°C) / Measured* BP (°C) Isobutane 3.21 -11.7 n-butane 19.58 -0.5 isobutylene 10.18 -6.9 cis-butene-2 27.82 0.8 trans-butene-2 27.82 0.8 butene-1 17.57 -1.3 1,3-butadiene 15.55 -4.4 * Experimental values are supplied by the MPBPWIN program database (EXP_MBVP.DB) which contains more than 11,000 organic compounds with reliably measured values which are taken from SRC's PHYSPROP Database. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the boiling range of this category are C4 hydrocarbons that are common across the 12 CAS numbers. Crude butadiene category products arise from

Boiling Point (Range)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	106-99-0 1,3-Butadiene 25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked 68513-68-8 Residues (Petroleum), Deethanizer Tower
Conclusion: (FT - CL)	Based on the calculated values, products in this category can have a boiling range of 3.21 to 27.82 °C. Based on the measured values, products in this category can have a boiling range of -11.7 to 0.8°C.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the MPBPWIN program and represent a potential boiling point range for products with the 12 CAS numbers listed under test substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. WSKOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "boiling point". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:

Boiling Point (Range)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Calculated Daphnid Acute Toxicity

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CRUDE BUTADIENE C4 ROBUST SUMMARY

Daphnid Acute Toxicity

Test Substance*:	Other TS
Method/Guideline*:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type):	Acute Daphnid Toxicity Calculation; LC50
GLP:	Not applicable
Year (study performed):	Not applicable
Species:	Daphnid (calculated toxicity values are not species specific)
Analytical Monitoring:	Not applicable
Exposure Period:	48 hours
Statistical Method: (FT - ME)*	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPIWIN computer model (2). KOWWIN also has a database of experimental Kow values (EXPKOW.DB). The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of toxicity data for component chemicals is an estimate of the potential toxicity of category products. Chemical — Calculated log K_{ow} — Measured* log K_{ow} Isobutane — 2.23 — 2.76 n-butane — 2.31 — 2.89 isobutylene — 2.23 — 2.34 cis-butene-2 — 2.09 — 2.31 trans-butene-2 — 2.09 — 2.33 butene-1 — 2.17 — 2.40 1,3-butadiene — 2.03 — 1.99 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values..

Calculated Daphnid Acute Toxicity

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4.

The seven chemicals selected to represent the daphnid acute toxicity range of this category are C4 hydrocarbons that are common across the 12 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 category can be found in the American Chemistry Council, Olefins Panel test plan for this category (3).

1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92.
2. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
3. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.

Results: (FT - RS)

Units/Value:

- **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

Calculated daphnid acute toxicity values for 7 chemicals representative of products in the Crude Butadiene C4 Category are as follows:

Chemical	Calculated log K_{ow}	Daphnid Acute 48-hr LC50 (mg/L)
Isobutane	2.23	28.51
n-butane	2.31	24.11
isobutylene	2.23	27.53
cis-butene-2	2.09	36.91
trans-butene-2	2.09	36.91
butene-1	2.17	31.21
1,3-butadiene	2.03	40.27

Chemical	Measured* log K_{ow}	Daphnid Acute 48-hr LC50 (mg/L)
Isobutane	2.76	9.39
n-butane	2.89	7.15
isobutylene	2.34	21.86
cis-butene-2	2.31	23.28
trans-butene-2	2.33	22.32
butene-1	2.40	19.28

Calculated Daphnid Acute Toxicity

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	1,3-butadiene 1.99 43.88 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.
Test Substance: (FT - TS)	106-99-0 1,3-Butadiene 25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked 68513-68-8 Residues (Petroleum), Deethanizer Tower
Conclusion: (FT - CL)	Based on the calculated Kow values, products in this category are expected to have a daphnid 48-hour LC50 range of 24.11 to 40.27 mg/L. Based on the measured Kow values, products in this category are expected to have a daphnid 48-hour LC50 range of 7.15 to 43.88 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The toxicity values are calculated.
Reference: (FT - RE)	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for " acute toxicity to aquatic invertebrates ". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CRUDE BUTADIENE C4 ROBUST SUMMARY

Fish Acute Toxicity

Test Substance*:	Other TS
Method/Guideline*:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type):	Acute Fish Toxicity Calculation; LC50
GLP:	Not applicable
Year (study performed):	Not applicable
Species:	Freshwater Fish (calculated toxicity values are not species specific)
Analytical Monitoring:	Not applicable
Exposure Period:	96 hours
Statistical Method: (FT - ME)*	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPIWIN computer model (2). KOWWIN also has a database of experimental Kow values (EXPKOW.DB). The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of toxicity data for component chemicals is an estimate of the potential toxicity of category products. Chemical — Calculated log K_{ow} — Measured* log K_{ow} Isobutane: 2.23 — 2.76 n-butane: 2.31 — 2.89 isobutylene: 2.23 — 2.34 cis-butene-2: 2.09 — 2.31 trans-butene-2: 2.09 — 2.33 butene-1: 2.17 — 2.40 1,3-butadiene: 2.03 — 1.99 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000

Calculated Fish Acute Toxicity

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

organic compounds with reliably measured values..

Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4.

The seven chemicals selected to represent the fish acute toxicity range of this category are C4 hydrocarbons that are common across the 12 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 category can be found in the American Chemistry Council, Olefins Panel test plan for this category (3).

1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92.
2. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
3. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.

Results: (FT - RS)

Units/Value:

- **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

Calculated fish acute toxicity values for 7 chemicals representative of products in the Crude Butadiene C4 Category are as follows:

Chemical	Calculated log K_{ow}	Fish Acute 96-hr LC50 (mg/L)
Isobutane	2.23	26.19
n-butane	2.31	22.03
isobutylene	2.23	25.28
cis-butene-2	2.09	34.23
trans-butene-2	2.09	34.23
butene-1	2.17	28.79
1,3-butadiene	2.03	37.59

Chemical	Measured* log K_{ow}	Fish Acute 96-hr LC50 (mg/L)
Isobutane	2.76	8.32
n-butane	2.89	6.28
isobutylene	2.34	19.93
cis-butene-2	2.31	21.26
trans-butene-2	2.33	20.36

Calculated Fish Acute Toxicity

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	butene-1 2.40 17.50 1,3-butadiene 1.99 40.98 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.
Test Substance: (FT - TS)	106-99-0 1,3-Butadiene 25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked 68513-68-8 Residues (Petroleum), Deethanizer Tower
Conclusion: (FT - CL)	Based on the calculated Kow values, products in this category are expected to have a fish 96-hour LC50 range of 22.03 to 37.59 mg/L. Based on the measured Kow values, products in this category are expected to have a fish 96-hour LC50 range of 6.28 to 40.98 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The toxicity values are calculated.
Reference: (FT - RE)	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for " acute toxicity to fish ". Selecting this option refers the reader to information in the "free text" field for "test substance".
FT - Free text
IUCLID fields include:
- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Calculated Fish Acute Toxicity

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CRUDE BUTADIENE C4 ROBUST SUMMARY

Hydrolysis (Stability in Water)

Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
Type (test type):	Not applicable
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Analytical Monitoring:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration preparation, vessel type, volume, replication, deviations from guideline or protocol**	Not applicable
Results: (FT - RS) **Units/Value:** • **Note: Analytical method, observations, half-lives by pH, degradation products**	Not applicable
Test Substance: (FT - TS)	106-99-0 1,3-Butadiene 25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked 68513-68-8 Residues (Petroleum), Deethanizer Tower

Hydrolysis (Stability in Water)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

Conclusion: (FT - CL)	**Summary** In the environment, hydrolysis will not contribute to the degradation of chemicals in the Crude Butadiene C4 category (C4 refers to a chemical with 4 carbons). This category includes three process streams: • **C4 Crude Butadiene** • **Butadiene Unit Heavy Ends** • **Full-Range Butadiene Concentrates** Twelve CAS numbers identify products derived from these process streams. As discussed below, the chemicals in these streams are composed of carbon and hydrogen and are not amenable to hydrolysis because of their molecular structure and the chemical reaction required for this type of transformation to occur. **The Crude Butadiene C4 Category** A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. Process streams containing 10 to 92% butadiene are referred to as "crude butadiene." With the exception of CAS 106-99-0 (which is pure 1,3-butadiene), the CAS numbers or streams in this category consist of complex mixtures of hydrocarbons. Most commercial products in this category have a carbon number distribution predominantly between C3 and C5. All of these streams contain significant levels of 1,3-butadiene and olefins, which is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Crude Butadiene C4. The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process). Crude butadiene streams arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the three process streams in this category are: • **C4 Crude Butadiene** is produced by the distillation of a condensed portion of cracked gas in an ethylene process. C4 Crude Butadiene typically contains 40% to about 60% 1,3-butadiene, but could contain between 10% and 82% butadiene. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons.

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

- **Butadiene Unit Heavy Ends** is produced by extractive distillation of cracked gas. The 1,3-butadiene content of this mixed stream ranges from 13% to 92%. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. Only three companies report isolating this stream which is more typically an un-isolated intermediate.

- **Full-Range Butadiene Concentrates** is produced from cracked gas after the removal of ethylene or ethylene and propylene. The 1,3-butadiene content of full range butadiene concentrates has been reported to range from 12% to 42%. Other chemicals in this mixed stream are those containing three to twelve or more carbons. These streams are intermediates that are not normally isolated in the ethylene process and have been reported as isolated only in infrequent situations.

Hydrolysis of Hydrocarbons as a Function of Molecular Structure

Hydrolysis of an organic molecule occurs when a molecule (R-X) reacts with water (H_2O) to form a new carbon-oxygen bond after the carbon-X bond is cleaved (2,3). Mechanistically, this reaction is referred to as a nucleophilic substitution reaction, where X is the leaving group being replaced by the incoming nucleophilic oxygen from the water molecule. The leaving group, X, must be a molecule other than carbon because for hydrolysis to occur, the R-X bond cannot be a carbon-carbon bond.

The carbon atom lacks sufficient electronegativity to be a good leaving group and carbon-carbon bonds are too stable (high bond energy) to be cleaved by nucleophilic substitution. Thus, hydrocarbons, including alkenes, are not subject to hydrolysis (3) and this fate process will not contribute to the degradative loss of chemical components in this category from the environment.

Under strongly acidic conditions the carbon-carbon double bond found in alkenes, such as those in the Crude Butadiene C4 category, will react with water by an addition reaction mechanism (2). The reaction product is an alcohol. This reaction is not considered to be hydrolysis because the carbon-carbon linkage is not cleaved and because the reaction is freely reversible (3).

Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (4). The chemicals in this category are primarily olefins that contain at least one double bond (alkenes). The remaining chemicals are saturated hydrocarbons (alkanes). These two groups of chemicals contain only carbon and hydrogen. As such, their molecular structure is not subject to the hydrolytic mechanism discussed above. Therefore, chemicals in the Crude Butadiene C4 category have a very low potential to hydrolyze, and this degradative process will not contribute to their removal in the environment.

Hydrolysis (Stability in Water)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	References 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA. 2. Gould, E.S. (1959), Mechanism and Structure in Organic Chemistry, Holt, Reinhart and Winston, New York, NY, USA. 3. Harris, J.C. (1982), "Rate of Hydrolysis," Chapter 7 in: W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, NY, USA. 4. Neely, W. B. 1985. Hydrolysis. In: W. B. Neely and G. E. Blau, eds. Environmental Exposure from Chemicals. Vol I., pp. 157-173. CRC Press, Boca Raton, FL, USA.
Reliability: (FT - RL)	Not applicable
Reference: (FT - RE)	American Chemistry Council, Olefins Panel. 2002. Hydrolysis: Crude Butadiene C4 Category. Rosslyn, VA, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "hydrolysis". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:
RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CRUDE BUTADIENE C4 ROBUST SUMMARY

Melting Point

Test Substance*:	Other TS
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Melting Point estimations performed by MPBPWIN are based on the average result of the calculation methods of K. Joback and Gold and Ogle. Joback's Method is described in Joback, K.G. 1982. A Unified Approach to Physical Property Estimation Using Multivariate Statistical Techniques. In The Properties of Gases and Liquids. Fourth Edition. 1987. R.C. Reid, J.M. Prausnitz and B.E. Poling, Eds. The Gold and Ogle Method simply uses the formula Tm = 0.5839Tb, where Tm is the melting point in Kelvin and Tb is the boiling point in Kelvin.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated MP (°C) / Measured* MP (°C) Isobutane: -132.55 / -138.3 n-butane: -120.28 / -138.2 isobutylene: -130.88 / -140.4 cis-butene-2: -120.41 / -105.5 trans-butene-2: -120.41 / -105.5 butene-1: -121.74 / -145.0 1,3-butadiene: -123.21 / -108.9 * Experimental values are supplied by the MPBPWIN program database (EXP_MBVP.DB) which contains more than 11,000 organic compounds with reliably measured values which are taken from SRC's PHYSPROP Database. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical

Melting Point (Range)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the melting range of this category are C4 hydrocarbons that are common across the 12 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	106-99-0 1,3-Butadiene 25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked 68513-68-8 Residues (Petroleum), Deethanizer Tower
Conclusion: (FT - CL)	Based on the calculated values, products in this category can have a melting range of -132.55 to -120.28 °C. Based on the measured values, products in this category can have a melting range of -145.0 to -105.5°C.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the MPBPWIN program and represent a potential melting range for products with the 12 CAS numbers listed under test substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. WSKOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

Melting Point (Range)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "melting point". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:
RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CRUDE BUTADIENE C4 ROBUST SUMMARY

Partition Coefficient

Test Substance*:	Other TS
Method/Guideline:	Calculated values using KOWWIN version 1.65, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Octanol / Water Partition Coefficient estimations performed by KOWWIN are based on an atom/fragment contribution method of W. Meylan and P. Howard in "Atom/fragment contribution method for estimating octanol-water partition coefficients". 1995. *J. Pharm. Sci*. **84**:83-92.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	See table below. * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the partition coefficient range of this category are C4 hydrocarbons that are common across the 12 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene

Chemical	Calculated log K_{ow}	Measured* log K_{ow}
Isobutane	2.23	2.76
n-butane	2.31	2.89
isobutylene	2.23	2.34
cis-butene-2	2.09	2.31
trans-butene-2	2.09	2.33
butene-1	2.17	2.40
1,3-butadiene	2.03	1.99

Partition Coefficient (Range)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	manufacturing. More information on the Crude Butadiene C4 category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	106-99-0 1,3-Butadiene 25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked 68513-68-8 Residues (Petroleum), Deethanizer Tower
Conclusion: (FT - CL)	Based on the calculated K_{ow} values, products in this category can have a partition coefficient range of 2.03 to 2.31. Based on the measured K_{ow} values, products in this category can have a partition coefficient range of 1.99 to 2.89.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the KOWWIN program and represent a potential partition coefficient range for products with the 12 CAS numbers listed under test substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "partition coefficient". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:
RL - Reliability

Partition Coefficient (Range)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CRUDE BUTADIENE C4 ROBUST SUMMARY

Photodegradation (Direct)

Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Type (air, soil, water, other):	Not applicable
Light Source:	Not applicable
Light Spectrum: • **Wave length value (upper/lower)**	Not applicable
Relative Intensity:	Not applicable
Test Substance Spectrum:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol**	Not applicable
Direct Photolysis:** **Results: half-life, % degradation, quantum yield**	**Summary** In the environment, photolysis will not significantly contribute to the degradation of chemicals in the Crude Butadiene C4 category (C4 refers to a chemical with 4 carbons). The Crude Butadiene C4 category includes three process streams: • **C4 Crude Butadiene** • **Butadiene Unit Heavy Ends** • **Full-Range Butadiene Concentrates** Twelve CAS numbers (Table 1) identify products derived from these process streams. As discussed below, the reaction process involved in direct photolysis occurs when sufficient light energy excites a molecule to the degree that a structural transformation occurs. In general, products in this category do not contain component chemicals (Table 2) that will undergo direct photolysis. **The Crude Butadiene C4 Category**

Photodegradation (Direct)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. Process streams containing 10 to 92% butadiene are referred to as "crude butadiene." With the exception of CAS 106-99-0 (which is pure 1,3-butadiene), the CAS numbers or streams in this category (Table 1) consist of complex mixtures of hydrocarbons (Table 2). Most commercial products in this category have a carbon number distribution predominantly between C3 and C5. All of these streams contain significant levels of 1,3-butadiene and olefins, which is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Crude Butadiene C4. The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process). Crude butadiene streams arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the three process streams in this category are: • **C4 Crude Butadiene** is produced by the distillation of a condensed portion of cracked gas in an ethylene process. C4 Crude Butadiene typically contains 40% to about 60% 1,3-butadiene, but could contain between 10% and 82% butadiene (Table 2). Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. • **Butadiene Unit Heavy Ends** is produced by extractive distillation of cracked gas. The 1,3-butadiene content of this mixed stream ranges from 13% to 92% (Table 2). Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. Only three companies report isolating this stream which is more typically an un-isolated intermediate. • **Full-Range Butadiene Concentrates** is produced from cracked gas after the removal of ethylene or ethylene and propylene. The 1,3-butadiene content of full range butadiene concentrates has been reported to range from 12% to 42% (Table 2). Other chemicals in this mixed stream are those containing three to twelve or more carbons. These streams are intermediates that are not normally isolated in the ethylene process and have been reported as isolated only in infrequent situations.

Photodegradation (Direct)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

Photolysis of Hydrocarbons

The direct photolysis of an organic molecule occurs when it absorbs sufficient light energy to result in a structural transformation (2). The reaction process is initiated when light energy in a specific wavelength range elevates a molecule to an electronically excited state. However, the excited state is competitive with various deactivation processes that can result in the return of the molecule to a non excited state.

The absorption of light in the ultra violet (UV)-visible range, 110-750 nm, can result in the electronic excitation of an organic molecule. Light in this range contains energy of the same order of magnitude as covalent bond dissociation energies (2). Higher wavelengths (e.g. infrared) result only in vibrational and rotational transitions, which do not tend to produce structural changes to a molecule.

The stratospheric ozone layer prevents UV light of less than 290 nm from reaching the earth's surface. Therefore, only light at wavelengths between 290 and 750 nm can result in photochemical transformations in the environment (2). Although the absorption of UV light in the 290-750 nm range is necessary, it is not always sufficient for a chemical to undergo photochemical degradation. Energy may be re-emitted from an excited molecule by mechanisms other than chemical transformation, resulting in no change to the parent molecule.

A conservative approach to estimating a photochemical degradation rate is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by the molecule (3). Saturated hydrocarbons do not absorb light above 200 nm. Some characteristic absorbance maxima (λ_{max}) and associated molar absorptivities (ε) for selected unsaturated hydrocarbons are shown below (2):

Direct Photolysis: (continued)**

Results: half-life, % degradation, quantum yield

Hydrocarbon	**l below 290 nm**		**l above 290 nm**	
	l_{max}	e	l_{max}	e
Ethylene	193	10,000		
1,3-Butadiene	217	2,090		
Benzene	255	215		
Naphthalene	221 270	100,000 5,000	311	250

Photodegradation (Direct)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	Olefins with one double bond, two conjugated double bonds, or multiple un-conjugated bonds, which constitute the majority of the chemicals in the Crude Butadiene C4 category, do not absorb appreciable light energy above 290 nm. The absorption of UV light to cause cis-trans isomerism about the double bond of an olefin occurs only if it is in conjugation with an aromatic ring (2). Single ring aromatics also do not absorb sufficient light energy above 290 nm to cause photolysis. However, fused aromatic ring systems such as naphthalene and PAHs absorb sufficient light energy above 290 to potentially result in photolysis (2). Except for naphthalene, which has been identified in one of the three process streams, products in this category do not contain component molecules of significant concentration (>2% by weight) that will undergo direct photolysis. Naphthalene irradiated at 313 nm has a quantum yield for photolysis of 0.015 and a half-life of 70 hours (4). In general, most products in the Crude Butadiene C4 category do not contain component molecules that will undergo direct photolysis. Therefore, this fate process will not contribute to a measurable degradative removal of chemical components in this category from the environment. **References** 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. Virginia, USA. 2. Harris, J. C. 1982. "Rate of Aqueous Photolysis," Chapter 8 in: W. J. Lyman, W. F. Reehl, and D. H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, USA. 3. Zepp, R. G. and D. M. Cline. 1977. Rates of Direct Photolysis in the Aqueous Environment, Environ. Sci. Technol., 11:359-366. 4. Zepp, R. G and P. F. Schlotzhauer. Photoreactivity of Selected Aromatic Hydrocarbons in Water, in Polynuclear Aromatic Hydrocarbons. P. W. Jones and P. Leber, eds., Ann Arbor Science Publishers, Inc., Ann Arbor, MI, USA. pp. 141-158.
Indirect Photolysis:** • **Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life**	Not applicable
Degradation Products:** • **Note: Identification,**	Unknown

Photodegradation (Direct)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

concentration	
Test Substance: (FT - TS)	106-99-0 1,3-Butadiene 25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked 68513-68-8 Residues (Petroleum), Deethanizer Tower
Conclusion: (FT - CL)	Not applicable
Reliability: (FT - RL)	Not applicable
Reference: (FT - RE)	American Chemistry Council, Olefins Panel. 2002. Hydrolysis: Crude Butadiene C4 Category. Rosslyn, VA, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "photodegradation". Selecting this option refers the reader to information in the "freetext" field for "test substance".
** In IUCLID, provide addtional discussion if needed in the results freetext
FT - Freetext
IUCLID fields include:
- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CRUDE BUTADIENE C4 ROBUST SUMMARY

Photodegradation (Indirect)

Test Substance*:	Other TS
Method/Guideline:	Calculated values using AOPWIN version 1.89, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Type (air, soil, water, other):	Not applicable
Light Source:	Sunlight
Light Spectrum: • **Wave length value (upper/lower)**	Natural sunlight
Relative Intensity:	1
Test Substance Spectrum:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol**	Indirect photodegradation, or atmospheric oxidation potential, is based on the structure-activity relationship methods developed by R. Atkinson. Temperature: 25°C Sensitizer: OH radical Concentration of Sensitizer: 1.5 E^6 OH radicals/cm^3
Direct Photolysis:** **Results: half-life, % degradation, quantum yield**	Not applicable
Indirect Photolysis:** • **Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life**	In the environment, organic chemicals emitted into the troposphere are degraded by several important transformation processes. The dominant transformation process for most compounds is the daylight reaction with hydroxyl (OH-) radicals (1,2). The rate at which an organic compound reacts with OH- radicals is a direct measure of its atmospheric persistence (3). AOPWIN estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The rate constants estimated by the program are then used to calculate atmospheric half-lives for organic compounds based upon average atmospheric

concentrations of hydroxyl radicals.

Since the reactions only take place in the presence of sunlight, the atmospheric half-lives are normalized for a 12-hour day.

Chemical	Calculated* half-life (hrs)	OH- Rate Constant (cm^3/molecule-sec)
Isobutane	52.6	2.4 E^{-12}
n-butane	48.8	2.6 E^{-12}
isobutylene	2.5	51.7 E^{-12}
cis-butene-2	2.3	56.7 E^{-12}
trans-butene-2	2.0	64.3 E^{-12}
butene-1	4.7	27.4 E^{-12}
1,3-butadiene	1.9	66.6 E^{-12}

* Atmospheric half-life values are based on a 12-hr day.

Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4.

The seven chemicals selected to represent the atmospheric half-life range of this category are C4 hydrocarbons that are common across the 12 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 category can be found in the American Chemistry Council, Olefins Panel test plan for this category (4).

References:

1. Atkinson, R. 1988. Estimation of gas-phase hydroxyl radical rate constants for organic chemicals. *Environ. Toxicol. Chem*. **7**:435-442.
2. Atkinson, R. 1989. Kinetics and mechanisms of the gas-phase reactions of the hydroxyl radical with organic compounds. J. Phys. Chem. Ref. Data Monograph No. 1, Amer. Inst. Physics & Amer. Chem. Soc., NY.
3. Meylan, W.M. and P.H. Howard. 1993. Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. *Chemosphere* **12**:2293-2299.
4. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.

Degradation Products:**	Unknown

Photodegradation (Indirect)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

• **Note: Identification, concentration**	
Test Substance: (FT - TS)	106-99-0 1,3-Butadiene 25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked 68513-68-8 Residues (Petroleum), Deethanizer Tower
Conclusion: (FT - CL)	Atmospheric oxidation vial hydroxyl radical can be a significant route of degradation for products in this category. Based on calculated values, products in this category can have an atmospheric half-life range of 1.9 to 52.6 hours as a result of indirect photolysis by hydroxyl radical attack.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include values calculated using the AOPWIN program and represent a potential atmospheric half-life range for products with the 12 CAS numbers listed under test substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. AOPWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "photodegradation". Selecting this option refers the reader to information in the "freetext" field for "test substance".
** In IUCLID, provide additional discussion if needed in the results freetext
FT - Freetext
IUCLID fields include:
RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CRUDE BUTADIENE C4 ROBUST SUMMARY

Transport / Distribution (Fugacity)

Test Substance*:	Other TS
Method/Guideline:	Calculated according to Mackay Level I, EQC Model version 1.01
Year (guideline):	1997
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. Physical properties input into the model are those calculated by the EPIWIN Estimation v 3.04 program (1) or supplied by the databases of experimental values contained with EPIWIN. Output data from the equilibrium model provides basic information on the potential distribution of chemicals between selected environmental compartments (i.e. air, water, soil, sediment, suspended sediment, biota). 1. EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of partitioning data for component chemicals is an estimate of the partitioning behavior for category products.

	Calculated* Percent Distribution		Measured** Percent Distribution	
Chemical	Air	Water	Air	Water
Isobutane	99.99	0.01	99.99	0.01
n-butane	99.98	0.02	99.99	0.01
isobutylene	99.98	0.02	99.99	0.01
cis-butene-2	99.97	0.03	99.98	0.02
trans-butene-2	99.97	0.03	99.98	0.02
butene-1	99.98	0.02	99.99	0.01

Transport / Distribution (Fugacity)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	1,3-butadiene 99.97 0.03 99.97 0.03 * Distribution values determined using input data calculated by the EPIWIN program **Distribution values determined using input data supplied by the EPIWIN program experimental databases (EXPKOW.DB, EXP_MBVP.DB, and EXP_MBVP.DB) which contain more than 11,000 organic compounds with reliably measured values. Distribution of each chemical to each remaining compartment (soil, sediment, suspended sediment, biota) was calculated as less than 0.01%. Mobility in the environment is expected to be high due to the relatively high water solubility and high vapor pressure of these chemicals. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the transport / distribution range of this category are C4 hydrocarbons that are common across the 12 CAS numbers and can represent a significant proportion of a product. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	106-99-0 1,3-Butadiene 25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked 68513-68-8 Residues (Petroleum), Deethanizer Tower

Transport / Distribution (Fugacity)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

Conclusion: (FT - CL)	Products in the Crude Butadiene C4 Category are expected to distribute to air with a small percentage partitioning to water.
Reliability: (FT - RL)	(2) Reliable with restrictions The input data used to run the EQC Level I model include estimated values calculated by the EPIWIN program based on chemical structure, and experimental values supplied by the EPIWIN program databases. The partitioning data represent a potential distribution range for products with the 12 CAS numbers listed under test substance. Computer modeling is an accepted method of assessing environmental distribution of chemicals.
Reference: (FT - RE)	Mackay, D.A. DiGuardo, S. Paterson, and C. Cowan. EQC Model Version 1.01. 1997. Available from the Environmental Modeling Centre, Trent University, Canada.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "transport / distribution". Selecting this option refers the reader to information in the "free text" field for "test substance".
FT - Free text
IUCLID fields include:
- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Vapor Pressure (Range)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CRUDE BUTADIENE C4 ROBUST SUMMARY

Vapor Pressure

Test Substance*:	Other TS
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Vapor Pressure estimations performed by MPBPWIN are based on the average result of the calculation methods of Antoine and Grain. Both methods use boiling point for the calculation. The Antoine Method is described in the Handbook of Chemical Property Estimation. Chapter 14. W.J. Lyman, W.F. Reehl and D.H. Rosenblatt, Eds. Washington, D.C.: American Chemical Society. 1990. A modified Grain Method is described on page 31 of Neely and Blau's Environmental Exposure from Chemicals, Volume 1, CRC Press. 1985.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated VP (hPa) / Measured* VP (hPa) Isobutane: 3.45 E^3 / 3.08 E^3 n-butane: 2.41 E^3 / 2.43 E^3 isobutylene: 2.97 E^3 / 3.08 E^3 cis-butene-2: 2.31 E^3 / 2.33 E^3 trans-butene-2: 2.31 E^3 / 2.33 E^3 butene-1: 2.48 E^3 / 3.00 E^3 1,3-butadiene: 2.73 E^3 / 2.81 E^3 * Experimental values are supplied by the MPBPWIN program database (EXP_MBVP.DB) which contains more than 11,000 organic compounds with reliably measured values which are taken from SRC's PHYSPROP Database. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a

Vapor Pressure (Range)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the vapor pressure range of this category are C4 hydrocarbons that are common across the 12 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	106-99-0 1,3-Butadiene 25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked 68513-68-8 Residues (Petroleum), Deethanizer Tower
Conclusion: (FT - CL)	Based on the calculated values, products in this category can have a vapor pressure range of 2.31 E^3 to 3.45 E^3 hPa. Based on the measured values, products in this category can have a vapor pressure range of 2.33 E^3 to 3.08 E^3 hPa.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the MPBPWIN program and represent a potential vapor pressure range for products with the 12 CAS numbers listed under test substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. WSKOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

Vapor Pressure (Range)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "vapor pressure". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:
RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

CRUDE BUTADIENE C4 ROBUST SUMMARY

Water Solubility

Test Substance*:	Other TS
Method/Guideline:	Calculated values using WSKOWWIN version 1.36, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Water Solubility estimations performed by WSKOWWIN are based on a Kow correlation method described by W. Meylan, P. Howard and R. Boethling in "Improved method for estimating water solubility from octanol/water partition coefficient". *Environ. Toxicol. Chem.* **15**:100-106. 1995.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated WS (mg/L) / Measured* WS (mg/L) Isobutane: 496.4 / 175.1 n-butane: 424.1 / 135.6 isobutylene: 495.6 / 399.2 cis-butene-2: 652.7 / 423.5 trans-butene-2: 652.7 / 407.1 butene-1: 557.7 / 354.8 1,3-butadiene: 732.4 / 792.3 * Experimental K_{ow} values supplied by the WSKOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the water solubility range of this category are C4 hydrocarbons that are common across the 12 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene

Water Solubility (Range)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

	manufacturing. More information on the Crude Butadiene C4 category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	106-99-0 1,3-Butadiene 25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked 68513-68-8 Residues (Petroleum), Deethanizer Tower
Conclusion: (FT - CL)	Based on the calculated K_{ow} values, products in this category can have a water solubility range of 424.1 to 732.4 mg/L. Based on the measured K_{ow} values, products in this category can have a water solubility range of 135.6 to 792.3 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include values estimated using calculated K_{ow} and experimental K_{ow} values available in the WSKOWWIN program and represent a potential water solubility range for products with the 12 CAS numbers listed under test substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. WSKOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "water solubility". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:
RL - Reliability

Water Solubility (Range)

CAS No.: 106-99-0; 25167-67-3; 68477-41-8; 68955-28-2; 68476-44-8; 68512-91-4; 68187-60-0; 68476-52-8; 68956-54-7; 69103-05-5; 64742-83-2; 68513-68-8

TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

COURTNEY M. PRICE
VICE PRESIDENT
CHEMSTAR

American Chemistry Council Good Chemistry Makes It Possible

October 14, 2003

Marianne Lamont Horinko
Acting Administrator
U.S. Environmental Protection Agency
P. O. Box 1473
Merrifield, VA 22116

RE: Olefins Panel Robust Summary for Crude Butadiene C4 Category Under the HPV Challenge Program
HPV Registration No.

Dear Ms. Horinko:

On May 4, 2000, the American Chemistry Council Olefins Panel (Panel) submitted a Test Plan under the High Production Volume (HPV) Chemical Challenge Program pertaining to the Crude Butadiene C4 Category. In the test plan, the Panel indicated that screening data for reproductive effects of 1,3-butadiene would become available. This information is now available and a robust summary for this information is attached. With this submission, the Panel has submitted robust summaries for all proposed studies and modeled or calculated parameters.

The Panel plans to submit a final report on the category in 2004.

If you have any questions, please contact Dr. Elizabeth Moran, Manager of the Olefins Panel at 301 924 2006 or Elizabeth_Moran@americanchemistry.com.

Sincerely yours,

Courtney M. Price
Vice President, CHEMSTAR

Attachments

cc: R. Hefter (EPA)

Toxicity to Reproduction

Test Substance	
Remarks	1,3-Butadiene CAS#: 106-99-0
Method	
Method/guideline followed	OECD 421 and OPPTS 870.3550
Test type	Inhalation reproduction/developmental toxicity screening test
GLP	Yes.
Year	2002
Species	Rat; Adults, 12 weeks old and weighing 342-409 grams (males) and 230-283 grams (females) at initiation of exposures
Strain	Crl:CD® (Sprague-Dawley) IGS BR
Route of administration	Inhalation (vapor).
Duration of test	Daily 6-hour exposures, beginning 14 days prior to initiation of the breeding period (15 exposures prior to breeding); F_0 males exposed for 83-84 consecutive days; F_0 females exposed through gestation day 20 and from lactation day 5 through the day prior to euthanasia (60-70 total days; F_0 females which did not deliver were exposed until one day prior to euthanasia (post-mating day 25); selected F_1 males and females (one male and one female from each litter) were exposed for 7 consecutive days (Postnatal days [PND] 21-27 or 28-34)
Doses/concentration levels	0, 300, 1500 and 6000 ppm
Sex	12 male, 12 female per group
Exposure period	6 hours/day
Frequency of treatment	7 days/week
Control group and treatment	12 male, 12 female, air-only exposed
Post exposure observation period	Daily; one hour following completion of exposure
Statistical methods	Parametric one-way analysis of variance (ANOVA) – body weight, body weight gain, food consumption, gestation length, precoital interval, number of pups born, live litter size, pup weights, organ weights (absolute and relative to final body weight), epididymal and testicular sperm numbers and sperm production rate; Chi-square test with Yates correction factor – mating and fertility indices; Kruskal Wallis with Mann-Whitney U test – sex ratios, postnatal survival, percentage of motile sperm with normal morphology
Test conditions	Three groups of F_0 animals, each consisting of 12 male and 12 female Crl:CD®(SD)IGS BR rats, were exposed to the test article, 1,3-butadiene, via whole body inhalation exposure for six hours daily for 14 days prior to the initiation of the breeding period and continuing throughout the gestation and lactation periods. A control group of identical design was

Test conditions (continued)	exposed to clean, filtered air on a comparable regimen. For F_0 dams, the daily inhalation exposures were suspended on gestation day 21 through lactation day 4, inclusively, in an attempt to avoid any confounding effects of exposure on nesting or nursing behavior; exposures were resumed for these dams on lactation day 5. The F_1 generation pups were potentially exposed to the test article *in utero*, and through nursing during lactation until weaning. Beginning on postnatal day (PND) 21, one male and one female from each litter were exposed for seven consecutive days to the same concentration of the test article as its dam. Beginning on PND 28, one previously unexposed male and one previously unexposed female per litter were exposed for seven consecutive days to the same concentration of the test article as its dam. Target test article concentrations were 300, 1500, and 6000 ppm (parts per million). All animals were observed twice daily (at least seven hours apart) for moribundity and mortality; weekly detailed physical examination data were collected for F_0 animals. Animals were observed for appearance, behavior, and pharmacotoxic signs prior to exposure, during exposure, and within one hour after completion of each daily exposure period. Body weights and food consumption data were recorded for males and females prior to treatment on the first day of exposure (body weights were also recorded at the midpoint of study week 1) and weekly thereafter until study termination for males and until gestation day 0 for females. During gestation, female body weights and food consumption were recorded on gestation days 0, 7, 14 and 20. Dams were monitored for signs of parturition and the day parturition was initiated was considered PND 0. For F_0 dams, body weights and food consumption data were collected on lactation days 1, 4, 7, 14, 21 and 28; data were collected weekly for F_0 males. Upon completion of delivery, all F_1 pups were individually identified; these offspring were observed daily for appearance, behavior and survival during the postnatal period. Detailed physical examinations and body weights were recorded for each pup on PND 1, 4, 7, 14, 21 and 28; food consumption was not recorded for F_1 pups. Pups were sexed on PND 0, 4, 7, 14, 21 and 28. Using a random selection process, litters were reduced to 10 pups (5/sex/litter, if possible), on PND 4. F_0 males and females received a detailed clinical examination on the day following their last exposure and were then euthanized by isoflurane inhalation. All F_0 animals were subjected to a complete macroscopic evaluation and selected organs were weighed. Designated tissues were examined

Test conditions (continued)	microscopically. A complete spermatogenesis evaluation was conducted for all F_0 males and included assessments of motility/viability, morphology, and sperm numbers for both the testis and epididymis. All F_1 offspring were euthanized and discarded without macroscopic pathological evaluation, with the exception of pups that were stillborn or those that died between birth and PND 4 and any pups that were considered moribund and euthanized in *extremis* during the lactation period. Macroscopic pathological evaluations were performed for these animals.
Results Actual mean exposure concentrations	301, 1507 and 6006 ppm
NOAEL	NOAEL (no-observed-adverse effect level) for F_0 parental and F_1 systemic toxicity for males and females directly exposed to the test article for six hours per day via whole-body inhalation: 300 ppm NOAEL for F_0 reproductive and F_1 developmental toxicity for F_0 males and females directly exposed to the test article for six hours per day via whole-body inhalation and F_1 offspring exposed to the test article *in utero* and directly for six hours per day via whole-body inhalation: 6000 ppm
Results (continued)	
LOAEL (LOEL)	Not applicable
F_0 and F_1 data (adverse responses/effects with NOAEL value)	Signs of chromodacryorrhea, chromorhinorrhea and salivation in F_0 males and females at 6000 ppm and infrequent occurrences of dried red material (perioral and perinasal regions) for four exposed F_1 offspring (three males and one female). Persistent reductions in body weight parameters for F_0 and F_1 males and females in the 1500 and 6000 ppm groups and transient reductions in food consumption (week 0-1) for F_0 males and females in these groups
Statistical Results (Test Article-Related Results with Statistical Significance [$p<0.05$ or $p<0.01$] Compared to the Control [0 ppm] Group)	6000 ppm Reduced F_0 male body weight Weeks 1 and 3-8 ($p<0.05$), reduced F_0 male body weight gain Weeks 0-1 ($p<0.01$) and 3-4 ($p<0.05$) and reduced cumulative F_0 male body weight gain Weeks 0-1 through 0-9 ($p<0.01$) and Weeks 0-10 and 0-11 ($p<0.05$) Transient reduced F_0 male g/animal/day and g/kg/day food consumption and food efficiency Week 0-1 ($p<0.01$);

Statistical Results (Test Article-Related Results with Statistical Significance [p<0.05 or p<0.01] Compared to the Control [0 ppm] Group) (continued)	increased F_0 male g/kg/day food consumption Weeks 5-6 through 8-9, 10-11 and 11-12 (p<0.01) due to lower body weights Reduced F_0 female g/kg/day food consumption Week 0-1 (p<0.05) Reduced F_0 female g/kg/day food consumption gestation days 0-7 (p<0.05) Reduced F_1 male body weight gain PND 23-24 (p<0.05) Reduced F_1 female body weight PND 25-28 (p<0.05), reduced F_1 female body weight gain PND 26-27 (p<0.05)and reduced F_1 female body weight gain PND 21-28 (p<0.01) Reduced F_1 male body weight gain PND 29-30 and 32-33 (p<0.01), reduced F_1 male body weight gain PND 28-35 (p<0.05) and reduced F_1 female body weight PND 33-35 (p<0.05) and body weight gain PND 28-35 (p<0.01) Increased F_0 male brain weight relative to final body weight (p<0.05); reduced F_0 male seminal vesicle/coagulating gland weight relative to brain weight (p<0.05) 1500 ppm F_0 male body weight gain Weeks 0-1 Reduced cumulative F_0 male body weight gain Weeks 0-7 (p<0.05 or p<0.01) Reduced F_0 male g/animal/day and g/kg/day food consumption Week 0-1 (p<0.05 and p<0.01, respectively); reduced F_0 male food efficiency Week 0-1 (p<0.01); increased F_0 male g/kg/day food consumption Weeks 6-7 through 11-12 (p<0.01) Reduced F_0 female g/kg/day food consumption Week 0-1 (p<0.05) Reduced F_0 female g/kg/day food consumption gestation days 0-7 (p<0.05) Reduced F_1 male body weight gain PND 29-30 and 32-33 (p<0.05) Reduced F_1 female body weight PND 27-28 (p<0.05)

Statistical Results (Test Article-Related Results with Statistical Significance [$p<0.05$ or $p<0.01$] Compared to the Control [0 ppm] Group) (continued)	Reduced F_1 female body weight gain PND 26-27 ($p<0.01$) and reduced F_1 female body weight gain PND 21-28 ($p<0.05$) Reduced F_1 female body weight PND 31 ($p<0.05$) and PND 32-35 ($p<0.01$) Reduced F_0 male seminal vesicle/coagulating gland weight relative to brain weight ($p<0.05$)
Remarks	Under the conditions of the current study, there were no adverse, test article-related effects on any parameter measured in either the F_0 or F_1 animals at the exposure level of 300 ppm. There was no test article-related mortality nor were there any apparent effects on gonadal function, mating behavior, conception, gestation, parturition, lactation of the F_0 generation at exposure levels up to 6000 ppm. There were no test article-related effects on the development of F_1 offspring from conception through weaning. In addition, no test article-related clinical findings were noted for F_1 animals directly exposed to the test article (via inhalation) at 300 or 1500 ppm. There were no effects on body weight parameters for F_1 males and females directly exposed to the test article at 300 ppm. There was an exposure-related increase in ejaculatory plugs, which had no apparent biological significance in this study. Test article-related effects that were considered adverse that were noted exclusively at 6000 ppm consisted of: Clinical observations indicative of chromodacryorrhea, chromorhinorrhea, and salivation in F_0 males and females. Occasional occurrences of dried red material (perioral and perinasal regions) in F_1 pups. Test article-related effects that were considered adverse that were noted at 1500 and 6000 ppm consisted of: Persistent reductions in body weight parameters in F_0 and F_1 males and females. Transient reductions in food consumption (week 0-1) for F_0 males and females. There were other test article-related observations in the F_0 generation that were not considered adverse. Clinical observations consistent with, but less severe than, those reported at 6000 ppm were also reported at 300 and 1500 ppm. These observations were not considered adverse at these lower levels because the signs were always transient and only

	reported during the one-hour post-exposure observations.
Conclusions	Based on the results of this study, an exposure level of 300 ppm was considered to be the NOAEL (no-observed-adverse-effect level) for F_0 parental systemic toxicity of 1,3-butadiene when rats were directly exposed to the test article for 6 hours per day via whole-body inhalation. The NOAEL for effects on gonadal function, mating behavior, conception, gestation, parturition, lactation of the F_0 generation, and the development of F_1 offspring from conception through weaning was considered to be 6000 ppm. The NOAEL for systemic toxicity for F_1 animals following postweaning 6-hour daily exposures (PND 21-27 or PND 28-34) was considered to be 300 ppm. There were no measurable differences between animals exposed from PND 21-27 and those exposed from PND 28-34.
References	NA
Other	NA
Last changed	12-Sept-03 Robust summary prepared by WIL Research Laboratories, Inc.

Toxicity to Reproduction

Test Substance	
Remarks	1,3-Butadiene CAS#: 106-99-0
Method	
Method/guideline followed	OECD 421 and OPPTS 870.3550
Test type	Inhalation reproduction/developmental toxicity screening test
GLP	Yes.
Year	2002
Species	Rat; Adults, 12 weeks old and weighing 342-409 grams (males) and 230-283 grams (females) at initiation of exposures
Strain	Crl:CD® (Sprague-Dawley) IGS BR
Route of administration	Inhalation (vapor).
Duration of test	Daily 6-hour exposures, beginning 14 days prior to initiation of the breeding period (15 exposures prior to breeding); F_0 males exposed for 83-84 consecutive days; F_0 females exposed through gestation day 20 and from lactation day 5 through the day prior to euthanasia (60-70 total days; F_0 females which did not deliver were exposed until one day prior to euthanasia (post-mating day 25); selected F_1 males and females (one male and one female from each litter) were exposed for 7 consecutive days (Postnatal days [PND] 21-27 or 28-34)
Doses/concentration levels	0, 300, 1500 and 6000 ppm
Sex	12 male, 12 female per group
Exposure period	6 hours/day
Frequency of treatment	7 days/week
Control group and treatment	12 male, 12 female, air-only exposed
Post exposure observation period	Daily; one hour following completion of exposure
Statistical methods	Parametric one-way analysis of variance (ANOVA) – body weight, body weight gain, food consumption, gestation length, precoital interval, number of pups born, live litter size, pup weights, organ weights (absolute and relative to final body weight), epididymal and testicular sperm numbers and sperm production rate; Chi-square test with Yates correction factor – mating and fertility indices; Kruskal Wallis with Mann-Whitney U test – sex ratios, postnatal survival, percentage of motile sperm with normal morphology
Test conditions	Three groups of F_0 animals, each consisting of 12 male and 12 female Crl:CD®(SD)IGS BR rats, were exposed to the test article, 1,3-butadiene, via whole-body inhalation exposure for six hours daily for 14 days prior to the initiation of the breeding period and continuing throughout the gestation and lactation periods. A control group of identical design was

Test conditions (continued)	exposed to clean, filtered air on a comparable regimen. For F_0 dams, the daily inhalation exposures were suspended on gestation day 21 through lactation day 4, inclusively, in an attempt to avoid any confounding effects of exposure on nesting or nursing behavior; exposures were resumed for these dams on lactation day 5. The F_1 generation pups were potentially exposed to the test article *in utero,* and through nursing during lactation until weaning. Beginning on postnatal day (PND) 21, one male and one female from each litter were exposed for seven consecutive days to the same concentration of the test article as its dam. Beginning on PND 28, one previously unexposed male and one previously unexposed female per litter were exposed for seven consecutive days to the same concentration of the test article as its dam. Target test article concentrations were 300, 1500, and 6000 ppm (parts per million). All animals were observed twice daily (at least seven hours apart) for moribundity and mortality; weekly detailed physical examination data were collected for F_0 animals. Animals were observed for appearance, behavior, and pharmacotoxic signs prior to exposure, during exposure, and within one hour after completion of each daily exposure period. Body weights and food consumption data were recorded for males and females prior to treatment on the first day of exposure (body weights were also recorded at the midpoint of study week 1) and weekly thereafter until study termination for males and until gestation day 0 for females. During gestation, female body weights and food consumption were recorded on gestation days 0, 7, 14 and 20. Dams were monitored for signs of parturition and the day parturition was initiated was considered PND 0. For F_0 dams, body weights and food consumption data were collected on lactation days 1, 4, 7, 14, 21 and 28; data were collected weekly for F_0 males. Upon completion of delivery, all F_1 pups were individually identified; these offspring were observed daily for appearance, behavior and survival during the postnatal period. Detailed physical examinations and body weights were recorded for each pup on PND 1, 4, 7, 14, 21 and 28; food consumption was not recorded for F_1 pups. Pups were sexed on PND 0, 4, 7, 14, 21 and 28. Using a random selection process, litters were reduced to 10 pups (5/sex/litter, if possible), on PND 4. F_0 males and females received a detailed clinical examination on the day following their last exposure and were then euthanized by isoflurane inhalation. All F_0 animals were subjected to a complete macroscopic evaluation and selected organs were weighed. Designated tissues were examined

Test conditions (continued)	microscopically. A complete spermatogenesis evaluation was conducted for all F_0 males and included assessments of motility/viability, morphology, and sperm numbers for both the testis and epididymis. All F_1 offspring were euthanized and discarded without macroscopic pathological evaluation, with the exception of pups that were stillborn or those that died between birth and PND 4 and any pups that were considered moribund and euthanized in *extremis* during the lactation period. Macroscopic pathological evaluations were performed for these animals.
Results Actual mean exposure concentrations	301, 1507 and 6006 ppm
NOAEL	NOAEL (no-observed-adverse-effect level) for F_0 parental and F_1 systemic toxicity for males and females directly exposed to the test article for six hours per day via whole-body inhalation: 300 ppm NOAEL for F_0 reproductive and F_1 developmental toxicity for F_0 males and females directly exposed to the test article for six hours per day via whole-body inhalation and F_1 offspring exposed to the test article *in utero* and directly for six hours per day via whole-body inhalation: 6000 ppm
Results (continued)	
LOAEL (LOEL)	Not applicable
F_0 and F_1 data (adverse responses/effects with NOAEL value)	Signs of chromodacryorrhea, chromorhinorrhea and salivation in F_0 males and females at 6000 ppm and infrequent occurrences of dried red material (perioral and perinasal regions) for four exposed F_1 offspring (three males and one female). Persistent reductions in body weight parameters for F_0 and F_1 males and females in the 1500 and 6000 ppm groups and transient reductions in food consumption (week 0-1) for F_0 males and females in these groups
Statistical Results (Test Article-Related Results with Statistical Significance [$p<0.05$ or $p<0.01$] Compared to the Control [0 ppm] Group)	<u>6000 ppm</u> Reduced F_0 male body weight Weeks 1 and 3-8 ($p<0.05$), reduced F_0 male body weight gain Weeks 0-1 ($p<0.01$) and 3-4 ($p<0.05$) and reduced cumulative F_0 male body weight gain Weeks 0-1 through 0-9 ($p<0.01$) and Weeks 0-10 and 0-11 ($p<0.05$) Transient reduced F_0 male g/animal/day and g/kg/day food consumption and food efficiency Week 0-1 ($p<0.01$);

Statistical Results (Test Article-Related Results with Statistical Significance [$p<0.05$ or $p<0.01$] Compared to the Control [0 ppm] Group) (continued)	increased F_0 male g/kg/day food consumption Weeks 5-6 through 8-9, 10-11 and 11-12 ($p<0.01$) due to lower body weights Reduced F_0 female g/kg/day food consumption Week 0-1 ($p<0.05$) Reduced F_0 female g/kg/day food consumption gestation days 0-7 ($p<0.05$) Reduced F_1 male body weight gain PND 23-24 ($p<0.05$) Reduced F_1 female body weight PND 25-28 ($p<0.05$), reduced F_1 female body weight gain PND 26-27 ($p<0.05$)and reduced F_1 female body weight gain PND 21-28 ($p<0.01$) Reduced F_1 male body weight gain PND 29-30 and 32-33 ($p<0.01$), reduced F_1 male body weight gain PND 28-35 ($p<0.05$) and reduced F_1 female body weight PND 33-35 ($p<0.05$) and body weight gain PND 28-35 ($p<0.01$) Increased F_0 male brain weight relative to final body weight ($p<0.05$); reduced F_0 male seminal vesicle/coagulating gland weight relative to brain weight ($p<0.05$) <u>1500 ppm</u> F_0 male body weight gain Weeks 0-1 Reduced cumulative F_0 male body weight gain Weeks 0-7 ($p<0.05$ or $p<0.01$) Reduced F_0 male g/animal/day and g/kg/day food consumption Week 0-1 ($p<0.05$ and $p<0.01$, respectively); reduced F_0 male food efficiency Week 0-1 ($p<0.01$); increased F_0 male g/kg/day food consumption Weeks 6-7 through 11-12 ($p<0.01$) Reduced F_0 female g/kg/day food consumption Week 0-1 ($p<0.05$) Reduced F_0 female g/kg/day food consumption gestation days 0-7 ($p<0.05$) Reduced F_1 male body weight gain PND 29-30 and 32-33 ($p<0.05$) Reduced F_1 female body weight PND 27-28 ($p<0.05$)

Statistical Results (Test Article-Related Results with Statistical Significance [$p<0.05$ or $p<0.01$] Compared to the Control [0 ppm] Group) (continued)	Reduced F_1 female body weight gain PND 26-27 ($p<0.01$) and reduced F_1 female body weight gain PND 21-28 ($p<0.05$) Reduced F_1 female body weight PND 31 ($p<0.05$) and PND 32-35 ($p<0.01$) Reduced F_0 male seminal vesicle/coagulating gland weight relative to brain weight ($p<0.05$)
Remarks	Under the conditions of the current study, there were no adverse, test article-related effects on any parameter measured in either the F_0 or F_1 animals at the exposure level of 300 ppm. There was no test article-related mortality nor were there any apparent effects on gonadal function, mating behavior, conception, gestation, parturition, lactation of the F_0 generation at exposure levels up to 6000 ppm. There were no test article-related effects on the development of F_1 offspring from conception through weaning. In addition, no test article-related clinical findings were noted for F_1 animals directly exposed to the test article (via inhalation) at 300 or 1500 ppm. There were no effects on body weight parameters for F_1 males and females directly exposed to the test article at 300 ppm. There was an exposure-related increase in ejaculatory plugs, which had no apparent biological significance in this study. Test article-related effects that were considered adverse that were noted exclusively at 6000 ppm consisted of: Clinical observations indicative of chromodacryorrhea, chromorhinorrhea, and salivation in F_0 males and females. Occasional occurrences of dried red material (perioral and perinasal regions) in F_1 pups. Test article-related effects that were considered adverse that were noted at 1500 and 6000 ppm consisted of: Persistent reductions in body weight parameters in F_0 and F_1 males and females. Transient reductions in food consumption (week 0-1) for F_0 males and females. There were other test article-related observations in the F_0 generation that were not considered adverse. Clinical observations consistent with, but less severe than, those reported at 6000 ppm were also reported at 300 and 1500 ppm. These observations were not considered adverse at these lower levels because the signs were always transient and only

	reported during the one-hour post-exposure observations.
Conclusions	Based on the results of this study, an exposure level of 300 ppm was considered to be the NOAEL (no-observed-adverse-effect level) for F_0 parental systemic toxicity of 1,3-butadiene when rats were directly exposed to the test article for 6 hours per day via whole-body inhalation. The NOAEL for effects on gonadal function, mating behavior, conception, gestation, parturition, lactation of the F_0 generation, and the development of F_1 offspring from conception through weaning was considered to be 6000 ppm. The NOAEL for systemic toxicity for F_1 animals following postweaning 6-hour daily exposures (PND 21-27 or PND 28-34) was considered to be 300 ppm. There were no measurable differences between animals exposed from PND 21-27 and those exposed from PND 28-34.
References	NA
Other	NA
Last changed	12-Sept-03 Robust summary prepared by WIL Research Laboratories, Inc.

US High Production Volume Chemical Program

Category Summary

For

Crude Butadiene C4 Category

Prepared by:

Olefins Panel of the American Chemistry Council

April 26, 2004

EXECUTIVE SUMMARY

The Olefins Panel of the American Chemistry Council (ACC) hereby submits the category summary report for the Crude Butadiene C4 Category under the Environmental Protection Agency's High Production Volume (HPV) Chemical Challenge Program (Program). The purpose of this report is to:

- Present results of an assessment to determine whether four production streams can be adequately characterized with existing data and additional data as described in the Crude Butadiene C4 Category test plan.
- Summarize the SIDS (Screening Information Data Set) physicochemical, environmental fate and effects, and human health HPV Program endpoints for the Crude Butadiene C4 Category.
- Provide a description of manufacturing processes, potential exposure sources, and uses for Crude Butadiene C4 streams.

The Crude Butadiene C4 Category originally contained four streams. After all data were evaluated to determine whether the streams formed a cohesive category, it was decided that two streams, Pyrolysis C3+ and Pyrolysis C4+, should be considered a separate category based on composition and effects of stream constituents, which are not shared by all four streams. Therefore, these two streams were removed from this category. A category summary report characterizing their HPV Program endpoints will be prepared and submitted separately. Consequently, the following category report summarizes HPV Program data for the C4 Crude Butadiene and Butadiene Unit Heavy Ends streams, which constitute the revised Crude Butadiene C4 Category.

The two streams retained in the Crude Butadiene C4 Category consist of a complex mixture of hydrocarbons. The typical carbon (C) number distribution for these streams ranges predominantly between C3 and C5. Much of the data used to characterize this category are from 1,3-butadiene, which is the most chemically reactive of the constituents and hence presumed the most biologically active component and major contributor to toxicological activity. This chemical is present in the two streams covered by this category at concentrations between approximately 10 to 92% (by weight).

Exposure

Industrial emissions of chemicals such as 1,3-butadiene are reported annually to the EPA and made available to the public in the Toxics Release Inventory (TRI). The TRI data indicate that industrial emissions of 1,3-butadiene have declined by 69% since 1988 or from 7.7 million pounds to 2.4 million pounds per year in 2000.

Fugitive emissions and other emission sources can result in the potential for low-level ambient air concentrations of constituents from the two streams at locations neighboring industrial facilities where they are manufactured. Both EPA and state agencies enforce a wide range of volatile organic compound and hazardous air pollutant environmental regulations that control these emissions. 1,3-Butadiene off-property concentrations from category streams will be further reviewed nationally by EPA as the Clean Air Act Section 112f residual risk provisions are implemented. These regulations on 1,3-butadiene emissions limit the potential for emissions of the streams in this HPV Category.

Human Health

Crude Butadiene C4 streams have a low order of acute toxicity. The components of Crude Butadiene C4 streams are gaseous at normal temperature and pressure; thus, ingestion or dermal absorption of this material is unlikely. Minimal effects were observed at concentrations of 5,300 mg/m^3.

Liquid Crude Butadiene C4 (test material was cooled in a dry ice bath) did not produce dermal or ocular irritation in rabbits. Exposure to liquid crude butadiene C4 is unlikely, as the components of

the streams in this category are gases at normal temperature and pressure.

A species difference in repeated dose toxicity of crude butadiene C4 was apparent between rats and mice. Minimal effects were reported in rat repeated dose toxicity tests exposed to several Crude Butadiene C4 streams (1,3-butadiene content ranging from 10 to 99.2%). The no observable adverse effect levels were the highest concentrations tested or 17,679; 20,000; or 25,100 mg/m^3 (8,000; 9,060; or 11,365 ppm, respectively) following 90, 36, or 9 days of exposure, respectively. In contrast, mortality was observed in mice exposed to 2,761 mg/m^3 1,3-butadiene (99.2%) for 90 days. Well documented species differences in 1,3-butadiene metabolism are the likely reason for the noted differences in repeat dose toxicity. Mice produce greater amounts of toxic metabolites following 1,3-butadiene exposure than rats. Available data suggest humans metabolize 1,3-butadiene similarly to rats.

Test data demonstrate that crude butadiene C4 can produce genotoxicity. *In vitro*, crude butadiene C4 demonstrated little activity in reverse mutation assays conducted in *Salmonella typhimurium* either in the presence or absence of metabolic activation. In addition, crude butadiene C4 did not increase the number of transformed foci in C3H/10T1/2 cloned 8 mouse embryo fibroblast cells. In the mouse lymphoma assay, evidence of mutagenic activity in mouse lymphoma L5178Y cells in culture was observed in the absence of metabolic activation, but not in the presence of metabolic activation. *In vivo*, several crude butadiene streams, containing 10 to 45% 1,3-butadiene, induced micronuclei formation in rats and mice following inhalation exposure.

No reproductive or developmental toxicity was observed in rats exposed to crude butadiene during the conduct of an OECD 422 repeat dose reproductive/developmental toxicity screen. Exposures to concentrations of 20,000 mg/m^3 were without effect. Further, in a prenatal developmental toxicity study, inhalation exposure of pregnant rats to 1,3-butadiene on days 5 to 16 (inclusive) of gestation elicited no developmental toxicity at any tested concentration up to 2,210 mg/m^3. Maternal toxicity was observed at levels of 442 mg/m^3. Similar to observations of species differences in repeat dose toxicity, mice were more sensitive than rats in developmental and reproductive toxicity following exposure to 1,3-butadiene. This increased sensitivity was apparent in effects on male germ cells observed in a dominant lethal study and an assessment of sperm morphology in male mice and fetal effects observed in a prenatal developmental toxicity study.

Environment

Results of distribution modeling show that chemical constituents of streams in the Crude Butadiene C4 Category will partition primarily to the air compartment, with a negligible amount partitioning to water. In the air, these constituents have the potential to rapidly degrade through indirect photolytic processes mediated primarily by hydroxyl radicals. This is expected to be the dominant route of loss and degradation process for constituents of these streams. Aqueous photolysis and hydrolysis will not contribute to the transformation of category constituents in aquatic environments because they are either poorly or not susceptible to these reactions.

Although the biodegradability of streams in this category has not been evaluated with standard testing procedures because of their high volatility, studies have demonstrated that several category constituents can be degraded by bacteria isolated from soil and surface water samples. The results from these studies show that selected stream constituents are subject to microbial degradation. However, biodegradation is unlikely to contribute to the overall degradation of constituents from these streams because they tend to partition to the air compartment.

Due to the fact that streams in this category are gaseous at ambient temperature and pressure and expected to partition predominantly to the atmosphere, aquatic toxicity testing was not conducted. However, aquatic toxicity was assessed with a model that is based on an equation developed for neutral organic chemicals, which is a reliable estimation method for the class of chemicals in streams from this category. Calculated toxicity values for two to four day exposures suggest that

category members have the potential to produce moderate toxicity, based on an effect range of 15.35 to 40.27 mg/L for selected stream constituents.

OLEFINS PANEL of the AMERICAN CHEMISTRY COUNCIL
MEMBER COMPANIES

ATOFINA Petrochemicals, Inc.*
BP Amoco, p.l.c.
Chevron Phillips Chemical Company LP
The Dow Chemical Company
E. I. du Pont de Nemours and Company
Eastman Chemical Company
Equistar Chemicals, LP
ExxonMobil Chemical Company
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The Goodyear Tire & Rubber Company
Huntsman Corporation
NOVA Chemicals Inc.
Noveon, Inc.*
Sasol North America, Inc.
Shell Chemical LP
Sunoco, Inc.*
Texas Petrochemicals LP
Westlake Chemical Corporation
Williams Olefins, LLC

* Companies that are part of the Olefins Panel, but do not produce Chemical Abstracts Service registration numbers in the Crude Butadiene C4 Category.

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1 CATEGORY DESCRIPTION AND JUSTIFICATION

1.1 Category Identification

For purposes of the U.S. High Production Volume (HPV) Chemical Challenge Program (Program), the Crude Butadiene C4 Category test plan submitted in May 2000 (Olefins Panel, HPV Implementation Task Group, 2000) included four production streams and eleven Chemical Abstracts Service (CAS) registration numbers (RNs) (Table 1). The test plan identified existing data and additional data to be developed, based on an extensive technical review of the category, to adequately characterize the four streams for the HPV Program endpoints. After the additional data were developed and all data evaluated to determine whether the streams formed a cohesive category as originally envisaged, it was decided that two streams, Pyrolysis C3+ and Pyrolysis C4+, should be considered as a separate category based on compositional differences and potential effects of stream constituents not shared by all four streams. Therefore, a category summary report that characterizes the HPV Program endpoints will be prepared and submitted separately for these two streams.

The following category report summarizes HPV Program data for the C4 Crude Butadiene and Butadiene Unit Heavy Ends streams, which constitute the revised Crude Butadiene C4 Category and contain ten CAS RNs (the CAS RNs listed in Table 1 except CAS RN 68513-68-8, which was shared exclusively by the Pyrolysis C3+ and Pyrolysis C4+ streams; a second CAS RN, 64742-83-2, is also shared by the C4 Crude Butadiene stream and will be retained in the revised category).

Table 1. Production Streams, CAS RNs, and CAS RN Names in the Crude Butadiene C4 Category

Production Streams	CAS RN	CAS RN Name
C4 Crude Butadiene	68476-52-8	Hydrocarbons, C4, Ethylene-Manuf.-By-Product
	68187-60-0	Hydrocarbons, C4, Ethane-Propane-Cracked
	68955-28-2	Gases, (Petroleum), Light Steam-Cracked, Butadiene Conc.
	64742-83-2	Naphtha, (Petroleum), Light Steam Cracked
	68476-44-8	Hydrocarbons, >C3
	68956-54-7	Hydrocarbons, C4, Unsatd.
	68477-41-8	Gases, Petroleum, Extractive, C3-5, Butadiene-Butene-Rich
	25167-67-3	Butene
Butadiene Unit Heavy Ends	69103-05-5	Hydrocarbons, C4-7, Butadiene Manuf. By-Product
	68477-41-8	Gases, Petroleum, Extractive, C3-5, Butadiene-Butene-Rich
	68512-91-4	Hydrocarbons, C3-4-Rich, Petroleum Distillates
Pyrolysis C3+	64742-83-2	Naphtha, (Petroleum), Light Steam Cracked
	68513-68-8	Residues, (Petroleum), Deethanizer Tower
Pyrolysis C4+	64742-83-2	Naphtha, (Petroleum), Light Steam Cracked

Note: The CAS numbers associated with corresponding production streams are shown in the above table. The definitions found in the TSCA Chemical Substance Inventory for the CAS RNs in this category are vague with respect to composition. Therefore, it is not uncommon to find that one CAS RN is used to describe different streams (different compositions) or that two or more CAS RNs are used to describe one stream (similar composition). Pyrolysis C3+ and Pyrolysis C4+, originally included in the C4 Crude Butadiene Category, will be considered as a separate category based on compositional and other differences.

The two commercial production streams, C4 Crude Butadiene and Butadiene Unit Heavy Ends, 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. Although the chemical composition of the streams can vary, the defining characteristic of the two streams is that each contains a mixture of chemicals from a reaction or separation activity in the Olefins Industry hydrocarbon processes and each contains 1,3-butadiene at a minimum concentration of approximately 10%.

The two streams in this category are composed of a complex mixture of hydrocarbons. The typical carbon (C) number distribution for these streams ranges predominantly between C3 and C5. The major stream in the category on a production volume basis is a C4 stream that contains between approximately 10 to 82% 1,3-butadiene and is referred to as "C4 Crude Butadiene". Both streams contain significant levels of C4 olefins and 1,3-butadiene in particular, which is the most biologically active constituent and the major contributor to toxicological activity. This commonality is the basis for considering the two streams as a category for purposes of the HPV Program.

The TSCA Chemical Substance Inventory definitions for the CAS RNs in this and in other categories from the Olefins Panel's HPV Program can be vague with respect to composition. Therefore, it is not uncommon that a CAS RN is correctly used to describe different streams (different compositions) or that two or more CAS RNs are used to describe one stream (similar composition or process). For this reason, the data matrix for this category was developed based on two compositionally differentiated process streams, rather than on the CAS RNs in this category.

The Crude Butadiene C4 Category streams arise from production processes associated with ethylene manufacturing (see Appendix I for a description of the ethylene and associated processes). The category stream names have changed since the test plan for this category was prepared in 2001. The change came as a result of a review and a decision by the Olefins Panel to use terminology that is more broadly applied throughout the industry. Briefly, the two process streams are:

(1) C4 Crude Butadiene stream is produced from the distillation of a liquefied portion cracked gas. This stream typically contains approximately 40 to 60% 1,3-butadiene (Table 2). However, it can contain as little as 10% or as much as 82% 1,3-butadiene. Other hydrocarbons in this stream are predominately C4. This stream was referred to as Butadiene Concentrate in the Crude Butadiene C4 Category Test Plan (Olefins Panel, HPV Implementation Task Group, 2001).

(2) Butadiene Unit Heavy Ends stream is produced from extractive distillation. This stream contains approximately 13 to 92% 1,3-butadiene (Table 2). Other hydrocarbons in this stream are predominately C4. This stream was referred to as High Butadiene Heavy Ends in the Crude Butadiene C4 Category Test Plan.

Table 2. Typical Constituent (wt%) Range in Streams of the Crude Butadiene C4 Category

Constituent	C4 Crude Butadiene Stream (wt %)	Butadiene Unit Heavy Ends Stream (wt %)
tert-Butyl Catechol	0 - 0.01	
Methanol	0.0 - 0.3	
Methylacetylene & Propadiene	0.0 - 2.3	
Ethyl- & Vinylacetylene	0.7 - 3.0	
Propylene	0.0 - 1.9	
Other C3 & Lighter Hydrocarbons	0.5 - 1.7	
Isobutane	0.4 - 22	
Isobutylene	0.5 - 29	
n-Butane	1.5 - 30	0.0 - 6.0
cis- & trans-Butene-2	3.5 - 54	5 - 50
Butene-1	2.5 - 25	0.0 - 4.0
1,3-Butadiene	10 - 82	13 - 92
1,2-Butadiene	0.0 - 1.4	0.0 - 2.0
Other C5 & Higher	0.0 - 8.0	
Vinylcyclohexene	0.0 - 1.0	
Isopentane		0.0 - 3.0
Other C8 Hydrocarbons		0.0 - 4.0

Note 1: The balance of these streams is expected to be other hydrocarbons that have boiling points in the ranges of the listed constituents.

Note 2: The ranges should not be considered to represent absolute limits for these streams. They represent the high and low reported values, and are industry typical limit values.

1.2 Purity/Impurities/Additives

A polymerization inhibitor (typically tertiarybutylcatechol, CAS RN 98-29-3, at 50 ppm) is usually added to Crude Butadiene C4 streams prior to shipment.

1.3 Physico-Chemical Properties

The two streams in this category are complex, containing many different hydrocarbons (Table 2), and can vary in composition not only between manufacturers but also for an individual manufacturer, depending on feedstock type and operating conditions. The seven constituents listed in Tables 3 and 4 comprise significant proportions of the two streams, which is why they were selected to represent the potential range of physico-chemical (PC) properties of the streams in this category. Therefore, these data can be used to adequately characterize the five PC endpoints of substances in this category for the HPV Program.

Table 3. Summary of Calculated Physico-Chemical Properties for Selected Chemicals Contained by Streams in the Crude Butadiene C4 Category

Chemical	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (hPa@ 25°C)	Log P_{ow}	Water Solubility (mg/L)
Isobutane	-132.6	3.2	3.45 E3	2.23	496.4
n-Butane	-120.3	19.6	2.41 E3	2.31	424.1
Isobutylene	-130.9	10.2	2.97 E3	2.23	495.6
cis-Butene-2	-120.4	27.8	2.31 E3	2.09	652.7
trans-Butene-2	-120.4	27.8	2.31 E3	2.09	652.7
Butene-1	-121.7	17.6	2.48 E3	2.17	557.7
1,3-Butadiene	-123.2	15.6	2.73 E3	2.03	732.4

Calculated values derived by the EPIWIN program (EPIWIN, 1999).

Table 4. Summary of Measured Physico-Chemical Properties for Selected Chemicals Contained by Streams in the Crude Butadiene C4 Category

Chemical	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (hPa@ 25°C)	Log P_{ow}	Water Solubility (mg/L)
Isobutane	-138.3	-11.7	3.08 E3	2.76	175.1
n-Butane	-138.2	-0.5	2.43 E3	2.89	135.6
Isobutylene	-140.4	-6.9	3.08 E3	2.34	399.2
cis-Butene-2	-105.5	0.8	2.33 E3	2.31	423.5
trans-Butene-2	-105.5	0.8	2.33 E3	2.33	407.1
Butene-1	-145.0	-1.3	3.00 E3	2.40	354.8
1,3-Butadiene	-108.9	-4.4	2.81 E3	1.99	792.3

Measured values from the EPIWIN experimental database (EPIWIN, 1999).

The following sections identify the values used to define the five PC endpoints of the two streams in this category.

1.3.1 Melting Point (Range)

Based on calculated values, the streams in this category can have a melting point range of -132.6 to -120.3 °C. Based on measured values, the streams in this category can have a melting point range of -145.0 to -105.5 °C. The calculated data compare favorably with the measured data. The measured data are considered the appropriate primary data set to characterize the melting point range of category members.

1.3.2 Boiling Point (Range)

Based on calculated values, the streams in this category can have a boiling point range of 3.2 to 27.8 °C. Based on measured values, the streams in this category can have a boiling point range of

-11.7 to 0.8 °C. The calculated data are not comparable with the measured data. The measured data are consistent with process knowledge and are considered the appropriate primary data set to characterize the boiling point range of category members.

1.3.3 Vapor Pressure (Range)

Based on calculated values, the streams in this category can have a vapor pressure range of 2.31 E3 to 3.45 E3 hPa at 25 °C. Based on measured values, the streams in this category can have a vapor pressure range of 2.33 E3 to 3.08 E3 hPa at 25 °C. The calculated data compare favorably with the measured data. The measured data are consistent with process knowledge and are considered the appropriate primary data set to characterize the vapor pressure range of category members.

1.3.4 Log P_{ow} (Range)

Based on calculated values, the streams in this category can have a log P_{ow} range of 2.03 to 2.31. Based on measured values, the streams in this category can have a log P_{ow} range of 1.99 to 2.89. The calculated data compare favorably with the measured data for the unsaturated molecules, 2.03 to 2.23 vs. 1.99 to 2.40, respectively. In comparison, the calculated data for the saturated molecules are not comparable with the measured data. The measured data are considered the appropriate primary data set to characterize the log P_{ow} range of category members.

1.3.5 Water Solubility (Range)

Based on calculated values, the streams in this category can have a water solubility range of 424.1 to 732.4 mg/L. Based on measured values, the streams in this category can have a water solubility range of 135.6 to 792.3 mg/L. As with the log P_{ow} data, the calculated data compare favorably with the measured data for the unsaturated molecules, 495.6 to 732.4 mg/L vs. 354.8 to 792.3 mg/L, respectively. In comparison, the calculated data for the saturated molecules are not comparable with the measured data. The measured data are considered the appropriate primary data set to characterize the water solubility range of category members.

1.4 Category Justification

Much of the data used to characterize human health endpoints of the two streams in the Crude Butadiene C4 Category are for 1,3-butadiene, which is the most chemically reactive of the constituents and hence presumed the most biologically active component and major contributor to toxicological activity. This chemical is present in the streams covered by this category at concentrations between approximately 10 to 92% (by weight). The presence of this chemical at concentrations $\geq$10% by weight presupposes that the stream would result in positive genotoxicity as the most sensitive endpoint. Supporting this presumption, two C4 Crude Butadiene stream samples, each with a different % 1,3-butadiene concentration (10 and 45%), have been shown to be genotoxic in mice.

At the time of this document's preparation, 1,3-butadiene has adequate quality data to characterize each HPV Program human health endpoint. Although an older acute inhalation toxicity study contained insufficient experimental detail to fully assess its quality, the results are consistent with the overall understanding of the hazard for this chemical. Therefore, the existing study was used to characterize the acute toxicity endpoint for 1,3-butadiene and to support the characterizaton of this category as a whole. There are also test data available for three different samples from the C4 Crude Butadiene stream. The composition of these samples was:

- 67% 1,3-butadiene; 30% butenes; 2% 1,2-butadiene; 1% other
- 45% 1,3-butadiene; 20% butanes; 30% butenes; 5% other

- 10% 1,3-butadiene; 29% 1-butene; 29% trans-2-butene; 12% cis-2-butene; 11% isobutylene; 4% n-butane; 4% isobutane; 1% other

Data for pure 1,3-butadiene together with data from two mid 1,3-butadiene-content C4 Crude Butadiene stream samples (approximately 45 and 67%) and one low 1,3-butadiene-content C4 Crude Butadiene stream sample (approximately 10%), adequately characterize the HPV Program human health effects endpoints for the two streams in this category.

2 EXPOSURE AND USE

The Crude Butadiene C4 Category contains 10 CAS RNs (Table 1) that are associated with the following two process streams:

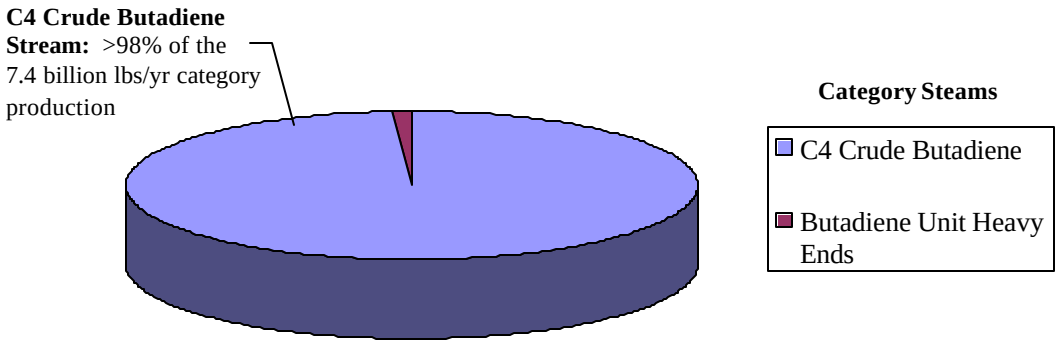
- C4 Crude Butadiene (referred to as Butadiene Concentrate in the Crude Butadiene C4 Category Test Plan)
- Butadiene Unit Heavy Ends (referred to as High Butadiene Heavy Ends in the Crude Butadiene C4 Category Test Plan)

These two streams are manufactured in ethylene production or butadiene finishing units (see Appendix II) and account for 100% of annual Crude Butadiene C4 Category production in the United States.

The C4 Crude Butadiene stream is a co-product of the ethylene manufacturing process and is processed at butadiene finishing units where it is separated into 1,3-butadiene and other 4-carbon (C4) chemicals. This stream accounts for over 98% of the 7.4 billion lbs/year (Figure 1), which was the total commercial production of streams in the Crude Butadiene C4 Category as reported by participants in the HPV Program based on their 1998 TSCA IUR reports. The balance of the category production consists of the Butadiene Unit Heavy Ends stream, which is recycled back into the production process or used as fuel in process furnaces. Subsequent processing of the streams in this category produces other substances (e.g., 1,3-butadiene) and the consumption of the original streams.

This category contains two Olefins Industry HPV streams that contain significant levels of 1,3-Butadiene (generally 10% by weight or greater). The C4 Crude Butadiene stream is transported in bulk by pipeline, barge, tank rail car, and infrequently by tank truck. There are no consumer uses of these streams and consequently no consumer exposure is expected.

Figure 1. Crude Butadiene C4 Category Production by Stream



For workers at ethylene and butadiene production plants where the streams in this category are manufactured and used, exposure to the streams is limited because processing occurs in closed systems. In addition, the Occupational Safety and Health Administration (OSHA) Butadiene Standard applies to these systems and thus limits worker exposure to the streams in this category. The Standard requires controls and work practices that limit 1,3-butadiene occupational exposure to less than 1 ppm, 8-hour TWA (time weighted average), and a short-term (15 minute) exposure of 5 ppm, which is the OSHA standard for 1,3-butadiene (OSHA, 1997). In addition, the OSHA Standard establishes an Action Level of 0.5 ppm (8-hour TWA), which effectively limits occupational exposure to 1,3-butadiene. Thus, the potential for occupational exposure to these streams is regarded to be minimal.

C4 Crude Butadiene, which accounts for approximately 98% of the production volume in the category, typically contains 50% 1,3-butadiene (reported concentrations of 1,3-butadiene in the C4 Crude Butadiene stream range from 10 to 82%). An 8-hour TWA and 15-minute STEL (Short Term Exposure Limit) occupational exposure to a typical C4 Crude Butadiene stream might approach 2 ppm and 10 ppm, respectively, for a facility complying with the OSHA 1,3-Butadiene Standard. Facilities that control below the Action Level of 0.5 ppm would have proportionally lower occupational exposures. For industrial workers at these facilities, the most likely exposure potential occurs through inhalation of low-level concentrations in air of vapors that escape from the closed process, such as fugitive emissions from valves and flanges; operations such as sampling, connecting, and disconnecting bulk transportation vessels (tank rail cars and barges); and during infrequent opening of equipment for maintenance.

Fugitive emissions and other emission sources can also result in the potential for low-level ambient air concentrations of the 2 category streams at locations neighboring the industrial facilities. Both EPA and state agencies enforce a wide range of volatile organic compound and hazardous air pollutant environmental regulations that control these emissions. Most industrial facilities (21 of 23 reporting sites) that produce or use these streams are located in the states of Texas or Louisiana. In Louisiana, the facilities are subject to an off-property 1,3-butadiene ambient air standard of 0.92 $\mu g/m^3$ (0.42 ppb) (Louisiana Department of Environmental Quality, 2003). Facilities in Texas are

subject to other requirements[1]. 1,3-Butadiene off-property concentrations resulting from category streams will be further reviewed nationally by EPA as the Clean Air Act Section 112f residual risk provisions are implemented. These regulations on 1,3-butadiene emissions limit the potential for emissions of the streams in this HPV Category.

Industrial emissions of chemicals such as 1,3-butadiene are reported annually to the EPA and made available to the public in the Toxics Release Inventory (TRI)[2]. The TRI is a publicly available EPA database that contains information on chemical releases and other waste management activities reported annually by selected industry groups as well as federal facilities. This inventory was established under the Emergency Planning and Community Right-to-Know Act of 1986 (EPCRA) and expanded by the Pollution Prevention Act of 1990.

The TRI data indicate that industrial emissions of 1,3-butadiene have significantly decreased since 1988 as production increased. 1,3-Butadiene production increased from 3.17 billion pounds in 1988 to 4.43 billion pounds in 2000 (Chemical and Engineering News; 1998, 2002). The TRI data from 2000 indicate that emissions of 1,3-butadiene declined by 69% since 1988 or from 7.7 million pounds to 2.4 million pounds per year in 2000. Similarly, Louisiana and Texas, where most of the 1,3-butadiene reporting industrial facilities are located, reported similar decreases in 1,3-butadiene TRI emissions since 1988: 69% and 67%, respectively, for total emissions and 69% and 63%, respectively, for air emissions.

The EPA National Toxics Inventory (NTI)[3] includes reported emissions of 1,3-butadiene. Emissions from streams in the Crude Butadiene C4 Category make up a part of the chemical sector's contribution to the NTI. The NTI includes emissions from major sources (e.g., chemical plants and oil refineries), area sources (e.g., gas stations), other stationary sources (e.g., wildfires and other prescribed burning), and mobile sources. Mobile sources include both on-road and off-road sources of emissions (e.g., cars, trucks, buses, off road vehicles, aircraft, locomotives, and commercial marine vessels).

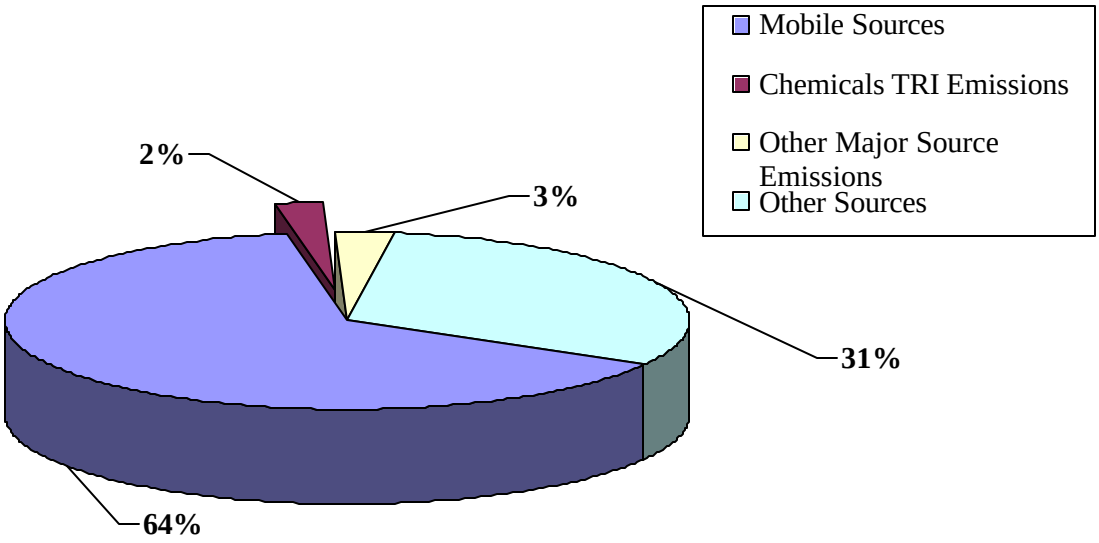
The 1996 NTI indicates total nationwide 1,3-butadiene emissions were 52,000 tons (104 million pounds). Major sources accounted for 5% of this total, mobile sources accounted for 64% and other sources made up the remaining 31%. The chemical sector's 1996 1,3-butadiene air emissions from the TRI data are a component of the NTI major source emissions, and equivalent to 2% of the total NTI emissions. These values are represented in Figure 2.

[1] 1,3-Butadiene monitoring data for Texas from the Community Air Toxics Monitoring Network can be found at: http://www.tnrcc.state.tx.us/air/monops/cat97/pdfs/97butadi13.pdf.

[2] EPA TRI website: http://www.epa.gov/tri/.

[3] Information concerning the EPA's NTI and their National Air Toxics Assessment can be found on the EPA Air Toxics website: http://www.epa.gov/ttn/atw/.

Figure 2. Percent 1,3-Butadiene Air Emissions by Source - 1996 Data



3 ENVIRONMENTAL FATE

3.1 Photodegradation

The atmosphere is the environmental compartment of interest when considering fate processes that can impact the persistence of streams in the Crude Butadiene C4 Category because they are gaseous. Results from an environmental distribution model support the assessment that chemical constituents of these streams will partition predominantly to the air compartment. The modelling results can be largely explained by the high vapor pressure of the constituents evaluated. In spite of their water solubility, wet deposition of category constituents is not likely to play a significant role in their atmospheric fate. Constituents of streams in this category have the potential to degrade at a significant rate in the atmosphere through indirect photolytic process mediated primarily by hydroxyl radicals (OH^-). In comparison, direct photolysis is not expected to contribute to the degradative fate of these streams in the aqueous environment.

3.1.1 Direct Photodegradation

The direct photolysis of an organic molecule occurs when it absorbs sufficient light energy to result in a structural transformation (Harris, 1982a). The reaction process is initiated when light energy at a specific wavelength elevates a molecule to an electronically excited state. However, the excited state is competitive with various deactivation processes that can result in the return of the molecule to a non excited state.

The absorption of light in the ultra violet (UV)-visible range, 110-750 nm, can result in the electronic excitation of an organic molecule. Light in this range contains energy of the same order of magnitude as covalent bond dissociation energies (Harris, 1982a). Higher wavelengths (e.g., infrared) result only in vibrational and rotational transitions, which do not tend to produce structural changes to a molecule.

The stratospheric ozone layer prevents UV light of less than 290 nm from reaching the earth's surface. Therefore, only light at wavelengths between 290 and 750 nm can result in photochemical

transformations in the environment (Harris, 1982a). Although the absorption of UV light in the 290-750 nm range is necessary, it is not always sufficient for a chemical to undergo photochemical degradation. Energy may be re-emitted from an excited molecule by mechanisms other than chemical transformation, resulting in no change to the parent molecule.

A conservative approach to estimating a photochemical degradation rate is to assume that degradation will occur in proportion to the amount of light at wavelengths >290 nm absorbed by the molecule (Zepp and Cline, 1977). Saturated hydrocarbons do not absorb light above 200 nm. Characteristic absorbance maxima (λ_{max}) and associated molar absorptivities (ε) for two unsaturated hydrocarbons, including 1,3-butadiene, are listed in Table 5 (Harris, 1982a).

Table 5. Characteristic Absorbance Maxima (λ_{max}) and Associated Molar Absorptivities (ε) for Two Unsaturated Hydrocarbons from Streams in the Crude Butadiene C4 Category

Hydrocarbon	λ below 290 nm	
	λ_{max*}	ε
Ethylene	193	10,000
1,3-Butadiene	217	20,900

* Values developed in organic solvents and regarded as approximate absorption maxima in aqueous solution.

Olefins with one double bond, two conjugated double bonds, or multiple un-conjugated bonds, which constitute the majority of the chemicals in the Crude Butadiene C4 Category, do not absorb appreciable light energy above 290 nm. Streams in this category do not contain constituent molecules of significant concentration that will undergo direct photolysis. Therefore, this fate process will not contribute to a measurable degradative removal of chemical constituents in this category from the environment.

3.1.2 Indirect Photodegradation

In the environment, organic chemicals emitted into the troposphere are degraded by several important transformation processes. The dominant transformation process for most compounds is the daylight reaction with hydroxyl (OH^-) radicals (Atkinson, 1988; Atkinson, 1989). The rate at which an organic compound reacts with OH^- radicals is a direct measure of its atmospheric persistence (Meylan and Howard, 1993).

AOPWIN estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The rate constants estimated by the program are then used to calculate atmospheric half-lives for organic compounds based upon an average atmospheric concentration of hydroxyl radicals.

Since the reactions necessary for this degradative process only take place in the presence of sunlight, the atmospheric half-lives are normalized for a 12-hour day. The seven chemicals selected to represent the atmospheric half-life range of streams in this category are C4 hydrocarbons that are predominant among the 10 CAS RNs (Table 6).

Atmospheric oxidation as a result of hydroxyl radical attack can be a significant route of degradation for streams in this category. Based on calculated values, streams in this category can have an atmospheric half-life range of 1.9 to 52.6 hours as a result of indirect photolysis by hydroxyl radical attack.

Table 6. Hydroxyl Radical Photodegradation Half-life of Selected Chemicals from Streams in the Crude Butadiene C4 Category

Chemical	Calculated Half-Life* (hrs)	OH^- Rate Constant (cm^3/molecule -sec)
Isobutane	52.6	2.4 E-12
n-Butane	48.8	2.6 E-12
Isobutylene	2.5	51.7 E-12
Cis-Butene-2	2.3	56.7 E-12
Trans-Butene-2	3.0	64.3 E-12
Butene-1	4.7	27.4 E-12
1,3-Butadiene	1.9	66.6 E-12

* Atmospheric half-life values are based on a 12-hr day and an OH^- concentration of 1.5E6, which is the default concentration used by the model.

3.2 Stability in Water (Hydrolysis)

Hydrolysis of an organic molecule occurs when a molecule (R-X) reacts with water (H_2O) to form a new carbon-oxygen bond after the carbon-X bond is cleaved (Gould, 1959; Harris, 1982b). Mechanistically, this reaction is referred to as a nucleophilic substitution reaction, where X is the leaving group being replaced by the incoming nucleophilic oxygen from the water molecule. The leaving group, X, must be a molecule other than carbon because for hydrolysis to occur, the R-X bond cannot be a carbon-carbon bond.

The carbon atom lacks sufficient electronegativity to be a good leaving group and carbon-carbon bonds are too stable (high bond energy) to be cleaved by nucleophilic substitution. Thus, hydrocarbons, including alkenes, are not subject to hydrolysis (Harris, 1982b) and this fate process will not contribute to the degradative loss of chemical constituents in this category from the environment.

Under strongly acidic conditions the carbon-carbon double bond found in alkenes, such as those in the Crude Butadiene C4 Category, will react with water by an addition reaction mechanism (Gould, 1959). The reaction product is an alcohol. This reaction is not considered to be hydrolysis because the carbon-carbon linkage is not cleaved and because the reaction is freely reversible (Harris, 1982b).

Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Neely, 1985). The chemicals in this category are primarily olefins that contain at least one double bond (alkenes). The majority of the remaining chemicals are saturated hydrocarbons (alkanes). These two groups of chemicals contain only carbon and hydrogen. As such, their molecular structure is not subject to the hydrolytic mechanism described above. Therefore, chemicals in the Crude Butadiene C4 Category have a very low potential to hydrolyze, and this degradative process will not contribute to their removal in the environment.

3.3 Distribution in the Environment

Fugacity-based multimedia modeling provides basic information on the relative distribution of a chemical between selected environmental compartments, which can include air, soil, water, sediment, suspended sediment, and biota. A widely used fugacity model, the EQC (Equilibrium Criterion) Level I model (Mackay *et al.*, 1996; Mackay, 1998) calculates chemical distribution between these compartments based on the input of basic physicochemical parameters including

molecular weight, water solubility, log P_{ow}, and melting point.

Results of the EQC Level I model (Table 7) for selected chemical constituents of streams from this category suggest that they will partition primarily to air, with a small percentage partitioning to water. These results can be explained by their high vapor pressure. Distribution of these chemicals to each remaining compartment (soil, sediment, suspended sediment, biota) is calculated as less than 0.01%.

The seven chemicals selected to characterize the transport/distribution range are C4 hydrocarbons that are predominant across the streams in this category. Physical property data (Table 4) used in the model are from the EPIWIN (1999) database.

Table 7. Environmental Distribution as Calculated by the EQC Level I Fugacity Model for Selected Chemicals from Streams in the Crude Butadiene C4 Category

Chemical	Distribution Per Environmental Compartment (%)					
	Air	Water	Soil	Sediment	Suspended Sediment	Biota
Isobutane	99.99	0.01	<0.01	<0.01	<0.01	<0.01
n-Butane	99.99	0.01	<0.01	<0.01	<0.01	<0.01
Isobutylene	99.99	0.01	<0.01	<0.01	<0.01	<0.01
cis-Butene-2	99.98	0.02	<0.01	<0.01	<0.01	<0.01
trans-Butene-2	99.98	0.02	<0.01	<0.01	<0.01	<0.01
Butene-1	99.99	0.01	<0.01	<0.01	<0.01	<0.01
1,3-Butadiene	99.97	0.03	<0.01	<0.01	<0.01	<0.01

Note: The distribution values were determined using physical property data from the EPIWIN (1999) database.

3.4 Biodegradation

Biodegradation is the use of a chemical by microorganisms as a source of energy and carbon. The parent chemical is broken down to simpler, smaller chemicals, which can be eventually converted to inorganic forms such as carbon dioxide, nitrate, sulfate, and water, depending on the composition of the parent chemical.

The microbial metabolism of aliphatic alkenes can be initiated by attack at the double bond (Watkinson and Morgan, 1990). Four degradative processes have been identified:

- Oxygenase attack upon a terminal methyl group to the corresponding alcohol, aldehyde, and acid
- Subterminal carbon oxygenase attack to the corresponding alcohol and ketone
- Oxidation across the double bond to the corresponding epoxide
- Oxidation across the double bond to the corresponding diol

Streams in the Crude Butadiene C4 Category are gaseous hydrocarbons, composed predominantly of chemicals with carbon numbers smaller than C5.

Constituent chemicals from the two process streams in this category are simple hydrocarbons (Table 2), the majority of which are calculated to partition primarily to the air where physical processes will contribute to their rapid degradation (see Indirect Photodegradation above for specific degradation rates of selected chemicals from this category). Consequently, their availability to microbial degraders can be significantly limited. Because of the partitioning behavior of

chemicals in this category, biodegradative processes will be less likely to contribute to their loss from the environment.

Streams from the Crude Butadiene C4 Category do not lend themselves to being evaluated for biodegradability using standard experimental designs because of their physical state. However, there is microbial metabolism information for several of the unsaturated C4 constituents in this category, including 1,3-butadiene, that demonstrates they have the potential to biodegrade. The sections immediately below summarize results of studies for selected constituents from this category. The data do not allow for an estimation of the extent of biodegradability relative to a standard 28-day test procedure using a microbial inoculum from a wastewater treatment facility. However, the constituents discussed below are predicted by BIOWIN, Biodegradation Probability Program (EPIWIN, 1999), as having the potential to biodegrade rapidly. [BIOWIN is a model in EPIWIN that calculates the probability of an organic chemical to rapidly biodegrade by a mixed population of microorganisms. BIOWIN can also estimate the time required to meet primary and ultimate biodegradation criteria.]

3.4.1 Propylene Biodegradation

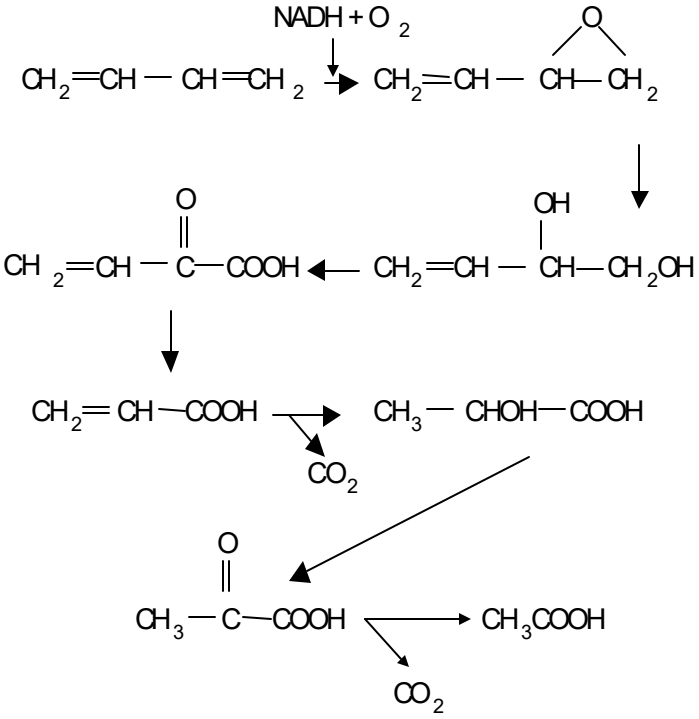
Propylene has been shown to be a growth substrate for several microorganisms. Isolated bacterial strains studied for their potential to biodegrade propylene under aerobic conditions were identified from the genus *Nocardia*, *Mycobacterium*, and *Xanthobacter* (de Bont *et al.*, 1980; de Bont *et al.*, 1982; de Bont *et al.*, 1983; van Ginkel and de Bont, 1986). Other species from the genus *Pseudomonas* and *Aerobacter* that were isolated from soil have also been associated with the ability to aerobically degrade propylene after they were shown to metabolize propylene oxide (Raja, 1991), an intermediate in the propylene metabolic pathway (van Agteren *et al.*, 1998).

Two pathways for the aerobic metabolism of propylene have been described (van Agteren *et al.*, 1998) that include the formation of either 1,2-propanediol or acetyl CoA prior to mineralization to CO_2.

3.4.2 1,3-Butadiene Biodegradation

Experimental studies to determine a catabolic pathway for 1,3-butadiene as mediated by a *Nocardia sp*. (Watkinson and Somerville, 1976) resulted in the series of reactions shown in Figure 3.

Figure 3. Proposed Microbial Metabolic Pathway for the Degradation of 1,3-Butadiene by a *Nocardia sp.*



The intermediary metabolic steps depicted in Figure 3 result in the production of acetic acid (CH_3COOH) which can be further metabolized. In addition, 1,3-butadiene has been estimated to have an aerobic aquatic biodegradation half-life ranging from 1 to 4 weeks (Howard *et al.,* 1991).

3.4.3 1-Butene Biodegradation

Isolated bacterial strains have been evaluated for their potential to biodegrade 1-butene under aerobic conditions. Bacteria from two genus, *Mycobacterium spp.* and *Xanthobacter spp.*, isolated from environmental samples have demonstrated the ability to degrade 1-butene (Hou *et al.*, 1983; Habets-Crützen *et al*., 1984; van Ginkel and de Bont, 1986; Weijers *et al*., 1995). Epoxybutane was shown to be converted to the corresponding ketone using a cell extract from a *Xanthobacter* spp. (Weijers *et al.*, 1995). These studies suggest that 1-butene can be biodegraded and that microbial metabolism can contribute to the overall loss of this chemical from the environment.

3.4.4 2-Butene Biodegradation

Although 2-butene has not been reported as a microbial growth substrate, an isolated bacterial strain, *Xanthobacter spp*., was evaluated for its potential to biodegrade various epoxyalkanes. Both diastereomeric forms of 2,3-expoxybutane were shown to degrade with degradation rates of 6 and 9 nmol/min/mg protein for trans- and cis- geometric isomers, respectively (Weijers *et al.*, 1988). These data suggest that a metabolic pathway is present in bacteria that will degrade these alkenes.

3.4.5 Isobutylene Biodegradation

Although isobutylene has not been reported as a growth substrate for bacteria, isolated bacterial strains have been evaluated for their potential to biodegrade 1-butene under aerobic conditions. Epoxybutane was shown to be converted to the corresponding ketone using a cell extract from a *Xanthobacter spp*.(Weijers *et al.*, 1995). In the same study, 2-methyl-1,2-epoxypropane was not converted suggesting that isobutylene metabolism is not mediated in a manner similar to 1-butene

by this organism. However, because of the structural similarity between 1-butene and isobutylene, isobutylene biodegradation may occur through a process not yet evaluated.

3.4.6 Abiotic and Biotic Degradation Summary

The stream constituents from this category will partition primarily to the air where physical degradative processes will dominate their fate. Data show that these chemicals are subject to rapid physical degradation. Selected constituents have also been shown to be subject to biodegradation. Overall, the constituent chemicals and consequently the streams from this category are expected to degrade rapidly in the environment from physical processes and not persist.

4 HUMAN HEALTH HAZARDS

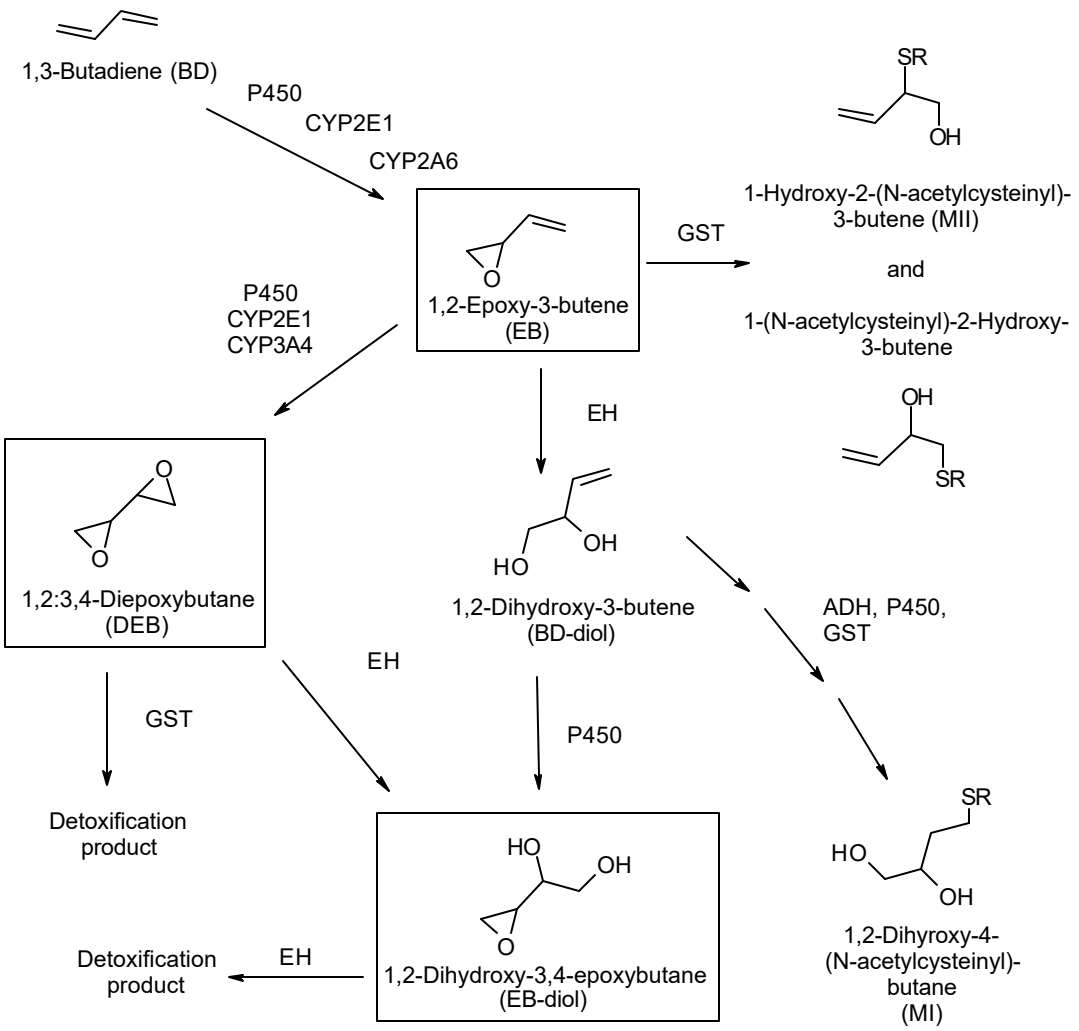
The two streams that comprise the Crude Butadiene C4 Category, which together contain ten CAS RNs, vary in 1,3-butadiene content, ranging from 10 to 92% 1,3-butadiene. Much of the data used to characterize the streams in this category are for 1,3-butadiene, which is the most biologically active constituent and thus the major contributor to toxicological activity. Therefore, data collected on 1,3-butadiene are included in the summaries below. The presence of this chemical at concentrations $\geq$10% by weight presupposes that the stream would result in positive genotoxicity as the most sensitive endpoint. Supporting this presumption, two samples from the Crude Butadiene C4 stream, containing 10 and 45% 1,3-butadiene, have been shown to be genotoxic. Data for pure 1,3-butadiene together with data from a mid 1,3-butadiene (approximately 45 to 67%) and a low 1,3-butadiene (approximately 10%) stream adequately characterize the HPV Program human health effects endpoints for the streams in this category.

4.1 Effects on Human Health

4.1.1 Toxicokinetics, Metabolism, and Distribution

1,3-Butadiene is initially oxidized to 1,2-epoxy-3-butene (EB), a reaction mediated primarily by P450 CYP 2E1 (Csanady *et al*., 1992; Duescher and Elfarra, 1994) (Figure 4). Further oxidation of EB produces 1,2:3,4-diepoxybutane (DEB) (Seaton *et al.*, 1995). Detoxification of EB proceeds by conjugation, mediated by glutathione-S-transferase (GST), or by hydrolysis, mediated by epoxide hydrolase (EH). Hydrolysis produces the 1,2-dihydroxy-3-butene (BD-diol) metabolite. Both DEB and BD-diol undergo further conversions *in vivo*, the former by EH mediated hydrolysis and the latter by P450 mediated oxidation, to produce the 1,2-dihydroxy-3,4-epoxybutane metabolite, known also as butadiene diol-epoxide (EB-diol) (reviewed in Himmelstein *et al.*, 1997). BD-diol can also be metabolized by P450 to hydroxymethylvinylketone (HMVK) (Kemper *et al.*, 1998), which may form $1N^2$-propanodeoxyguanosine DNA adducts *in vitro*. (Powley *et al*., 2003). EB, DEB, EB-diol, and HMVK are reactive electrophilic compounds with the potential to form carcinogenic intermediates from 1,3-butadiene metabolism *in vivo*.

Figure 4. Partial metabolic scheme for 1,3-butadiene (taken from Albertini *et al.*, 2003).



Direct GST mediated conjugation of EB with glutathione (GSH) leads to two detoxification products. One of these (i.e., 1-hydroxy-2-(N-acetylcysteinyl)-3-butene, also known as the urinary MII compound), as an isomeric mixture with 1-(N-acetylcysteinyl)-2-hydroxy-3-butene, is a biomarker of the conjugation detoxification pathway. GST mediated conjugation of HMVK with GSH leads to the production of 1,2-dihydroxy-4-(N-acetylcysteinyl)-butane (also known as the urinary MI compound). MI is a biomarker of the hydrolytic pathway because this detoxification pathway for EB is mediated initially by EH. The ratio MI/(MI + MII) in urine defines the relative importance of hydrolysis vs. conjugation in detoxification of EB (Bechtold *et al.*, 1994; reviewed in Henderson *et al.*, 1996).

In vitro studies have shown that mice are 2- and 10-fold more efficient than rats in oxidizing 1,3-butadiene to EB (Schmidt and Loeser, 1985; Csanady *et al.*, 1992). Furthermore, the second oxidation step to DEB could be mediated *in vitro* only by mouse liver microsomes (Csanady *et al.*, 1992). *In vivo* studies of 1,3-butadiene metabolism in mice and rats have also shown large inter-species differences. MI/(MI + MII) ratios in urine for mice and rats exposed to 1,3-butadiene by inhalation indicate that conjugation detoxification predominates in mice but that hydrolysis is more important in rats (Henderson *et al.*, 1996).

In summary, mice are more efficient in oxidation of 1,3-butadiene to electrophilic metabolites (especially to DEB), while rats are more efficient in hydrolytic detoxification. The existing metabolism data suggest that metabolism in humans appears to be more like metabolism in rats than in mice.

4.1.2 Acute Toxicity

Data are available to evaluate acute toxicity of streams in the Crude Butadiene C4 Category. As the streams are gaseous at room temperature, data are from inhalation toxicity studies (Table 8).

Table 8. Summary of Acute Inhalation Toxicity Data

CAS RN and Stream/Chemical Name (% 1,3-Butadiene)	Test Organism	Exposure Duration (hr)	LC_{50} (mg/m^3)
68955-28-2 C4 Crude Butadiene (45)	Rat	4	5,300
106-99-0 1,3-Butadiene (>99)	Rat	4	285,000
106-99-0 1,3-Butadiene (>99)	Mouse	2	270,000

Inhalation

Studies in Animals

Rats (5/sex) were exposed to 5,300 mg/m^3 of butadiene concentrate (CAS # 68955-28-2: 45% 1,3-butadiene; 20% butanes; and 30% butenes) in air for four hours (Gulf Oil Chemical Co., 1985). Clinical observations and body weights were recorded for fourteen days following exposure. No mortality was observed at this concentration and all rats appeared normal on days 2 to 14. Clinical observations included respiratory sounds in 2 male rats post exposure and minimal porphyrin around the eyes in one female rat. Necropsy revealed one female rat with an ovary filled with red fluid. The LC_{50} was >5,300 mg/m^3.

In a poorly reported study, LC_{50} values for 1,3-butadiene were determined to be 285,000 mg/m^3 (129,000 ppm) and 270,000 mg/m^3 (122,000 ppm) for rats (4 hr) and mice (2 hr), respectively (Shugaev, 1969).

Conclusion

Available data adequately address the acute toxicity of the Crude Butadiene C4 Category for the relevant route of inhalation exposure. Streams in this category are gaseous at room temperature. Acute inhalation toxicity tests have been conducted for streams containing either 45 or 100% 1,3-butadiene. No toxicity was observed for exposures up to 5,300 mg/m^3.

4.1.3 Irritation

Skin and eye irritation of Crude Butadiene C4 Category has been examined in rabbits.

Skin Irritation

Studies in Animals

In an irritation screening study, 0.1 ml of butadiene concentrate (CAS# 68955-28-2: 67% 1,3-butadiene; 30% butenes; and 2% 1,2-butadiene) was applied to the skin of one male and one female

New Zealand White rabbit (Mobil Environmental and Health Science Laboratory, 1985). The application site was occluded with a rubber dam. No irritation was observed at 1, 3, or 7 days after dosing.

Eye Irritation

Studies in Animals

In an irritation screening study, 0.1 ml of butadiene concentrate (CAS# 68955-28-2: 67% 1,3-butadiene; 30% butenes; and 2% 1,2-butadiene) was applied to the eye of one male and one female rabbit (Mobil Environmental and Health Science Laboratory, 1985a). Test stream was stored on dry ice prior to administration. No irritation was observed at 1, 3, or 7 days after dosing.

Conclusion

Butadiene concentrate is nonirritating to rabbit skin and eyes. Lack of irritation may be due to non irritating properties of the test stream or rapid removal of test stream from the application site by evaporation.

4.1.4 Repeated Dose Toxicity

Repeated dose toxicity tests have been conducted on a variety of streams in this category (Table 9). These studies range from 9 to 98 days in duration and have been conducted in rats and mice.

Table 9. Summary of Repeated Dose Toxicity Data

CAS RN and Stream Name (% 1,3-Butadiene)	Test Organism	Exposure Duration (days)	NOAEL (mg/m^3)
68476-52-8 C4 Crude Butadiene (10)	Crl:CD Rat	36	>20,000
106-99-0 1,3-Butadiene (>99)	CD Rat	91	>17,679
68955-28-2 C4 Crude Butadiene (45)	Fischer 344 Rat	9	>25,100
106-99-0 1,3-Butadiene (>99)	B6C3F1 Mouse	98	>2,760

Inhalation

Studies in Animals

Effects of repeated exposure to C4 Crude Butadiene (CAS# 68476-52-8: 10% 1,3-butadiene; 4% isobutane; 29% trans-2-butene; 29% 1-butene; 11% isobutylene; and 12% cis-2-butene) were evaluated as part of an OECD 422, Repeated Exposure Reproductive/Developmental Toxicity Screen in Crl:CD rats (Carney *et al.*, 2001). Twelve male and female rats were exposed to vapor concentrations 0; 2,000; 10,000; or 20,000 mg/m^3 Crude Butadiene for 36 or 37 days, 6 hr/da, 7 da/wk (this study contained an additional group of twelve female rats for reproductive and developmental toxicity screening evaluation). Males and females were sacrificed at the end of exposure. Effects on general toxicity, neurobehavioral activity, clinical chemistry, and hematology were evaluated. At necropsy, organs were weighed, evaluated grossly and histopathological evaluation was conducted. No deaths or treatment related clinical observations were reported. No treatment related changes were observed in body weight, sensory evaluation, rectal temperature,

fore/hindlimb grip performance, motor activity total counts, hematology, prothrombin time, clinical chemistry, organ weights, gross pathology, or histopathology. In evaluation of motor activity, the treatment-by-time by epoch interaction was significant. However, further evaluation indicated that this difference could be attributed to the time by epoch interaction rather than a treatment related effect. Females in the 2,000 mg/m^3 dose group had an increased hematocrit and a decrease in serum protein. However, these effects did not demonstrate a dose response and were not observed in males at the same dose level. As such these findings were considered incidental and not indicative of a treatment related response. The NOAEL in this study was 20,000 mg/m^3.

In a ninety-day repeat dose study, groups of 40 male and 40 female CD rats were exposed to 0; 2,209; 4,417; 8,334; or 17,679 mg/m^3 (0; 1,000; 2,000; 4,000; or 8,000 ppm, respectively) 1,3-butadiene (>99.2%, containing 120 ppm t-butyl catechol). Exposures were conducted for 6 hr/da, 5 da/wk for 13 weeks (Crouch *et al.*, 1979). Interim sacrifices of 10 rats/sex/group were conducted at 2 and 6 weeks, with blood being collected from all rats at these intervals and at terminal sacrifice. Body weights and food consumption were recorded weekly. Brain cholinesterase activity was determined in 5 rats/sex/group at the 2 and 6 week sacrifices and all rats at terminal sacrifice. Urine samples were collected from rats 1 to 2 weeks prior to sacrifice. Organ weights were determined for select organs with histopathology conducted on control and high exposure animals. Increased salivation was observed in female rats following 8 weeks of exposure. Decreased grooming was observed in male rats following ten weeks of exposure. Slight, non significant, reductions in body weight were observed in male rats. Organ weight and organ to brain weight ratios showed some scattered statistically significant differences among the groups but did not follow any consistent dose response trend. The NOAEL in this study was determined to be 17,679 mg/m^3.

No adverse effects were observed in rats following exposure to butadiene feedstock (CAS # 68955-28-2: 45% 1,3-butadiene; 20% butanes; and 30% butenes) in a well conducted short term repeated exposure study (Gulf Oil Chemicals Co., 1983a). Five male and five female Fischer 344 rats were exposed to 0; 2,500; or 25,100 mg/m^3 butadiene feedstock 6 hr/da, for a total of 9 days. Evaluations include body weight measurement, gross necropsy, organ weights, histopathology on selected organs, hematology, and clinical chemistry. With the exception of nasal discharge, no exposure related changes were observed. The NOAEL in this study was determined to be 25,100 mg/m^3.

Groups of 10 B6C3F1 mice/sex/group were exposed to 0; 1,380; 2,761; 5,522; 11,040; or 17,670 mg/m^3 (0; 625; 1,250; 2,500; 5,000; or 8,000 ppm, respectively) 1,3-butadiene (98.94% with 0.02% t-butyl catechol) 6 hr/da, 5 da/wk for 14 weeks (National Toxicology Program, 1984). Limited observations were conducted and included mortality and morbidity, body weight changes, gross pathology, and histolopathology on high dose and control animals. Mortality was observed in the 2,761 mg/m^3 group (1/10 males) and higher concentrations. Body weights were decreased at 5,522 mg/m^3 and higher concentrations. Despite mortality present at this concentration, the NOAEL was determined to be 2,761 mg/m^3.

Conclusion

Data are available to adequately characterize the repeated dose toxicity of Crude Butadiene C4 Category. The available studies were conducted by inhalation, the most appropriate route of exposure. Available studies cover a wide range of 1,3-butadiene concentrations (10 to 99%) in the test streams. The data are consistent in that they demonstrate minimal effects in rats with the exception of body weight changes following repeated inhalation exposures.

4.1.5 Mutagenicity

Genetic toxicity of crude butadiene has been evaluated both *in vitro* and *in vivo*. *In vitro* assays include Ames *Salmonella* Reverse Mutation assay, unscheduled DNA synthesis in rat hepatocytes, mammalian cell transformation assay, and mouse lymphoma assay. Potential for the *in vivo*

induction of chromosomal aberrations has been examined in rats and mice following inhalation exposure.

In vitro Studies

Studies in Animals

Mutagenic activity of 1,3-butadiene (CAS # 106-99-0) was evaluated in the Ames *Salmonella* Reverse Mutation assay (Arce *et al*., 1990). *Salmonella typhimurium* tester strains TA 97, TA 98, TA 100, and TA 1535 were overlaid on agar with or without mouse, rat, or human S9 activation systems in specially designed treatment chambers. 1,3-Butadiene gas was metered into the chambers at concentrations of 0, 30, 40, 50, and 60% for a 48-hour exposure period. An increase (just over 2-fold) in revertant colonies was observed only with the TA 1535 strain, all other strains demonstrated no increase. In this bacterial strain, mouse S9 had slightly higher activity than the uninduced rat or human S9 at 30% 1,3-butadiene in air. At concentrations greater than 30%, the number of revertants decreased in the presence of rat or human S9. Presence of human S9 did not substantially increase the number revertants compared to non S9 activated samples. Arochlor 1254 induced rat liver S9 fractions produced the same number of revertants as untreated mouse liver S9. Increasing the amount of rat S9 protein/plate slightly increased the number of revertants/plate without Arochlor 1254 induction, but did not produce an increase with Arochlor 1254 induction. In summary, 1,3-butadiene demonstrated weak mutagenic activity in this test system.

Butadiene concentrate (CAS # 68955-28-2: 67% 1,3-butadiene; 30% butenes; and 2% 1,2-butadiene) was evaluated for mutagenicity in the Ames *Salmonella* Reverse Mutation assay (Mobil Environmental and Health Sciences Laboratory, 1985b). Five strains of *Salmonella typhimurium* (TA 98, TA 100, TA 1535, TA 1537, and TA 1538) were incubated with 25, 50, 75, or 100 µl crude butadiene with and without Arochlor 1254 rat liver S9 activating system. Reversion frequencies in treated groups with and without S9 activation were similar to controls. The test stream was judged to be non mutagenic.

Butadiene concentrate (CAS# 68955-28-2: 45% 1,3-butadiene; 20% butanes; and 30% butenes), did not induce cell transformations in BALB/3T3-A31-1-1 cells treated *in vitro* with up to 20,000,000 mg/m^3 of the test stream (Gulf Oil Chemicals Co., 1983b). An increase in mutant frequency was observed in the mouse lymphoma cells following exposure to butadiene concentrate (CAS# 68955-28-2: 67% 1,3-butadiene; 30% butenes; and 1.2% 1,2-butadiene) in the absence of S9 activation. No increase was observed in the presence of S9 activating system (Mobil Environmental and Health Sciences Laboratory, 1985c). Unscheduled DNA synthesis (UDS) was observed in primary rat hepatocytes at 20,000,000 mg/m^3 butadiene concentrate (CAS# 68955-28-2: 45% 1,3-butadiene; 20% butanes; and 30% butenes), a level where marked cytotoxicity was observed (Gulf Oil Chemicals Co., 1984a) potentially confounding the data. No UDS was observed at treatment levels less than or equal to 10,000,000 mg/m^3.

In vivo Studies

Studies in Animals

Six male and female B6C3F1 mice were exposed to concentration of 500, 10,000, or 20,000 mg/m^3 C4 crude butadiene (CAS #, 68476-52-8: 10% 1,3-butadiene; 4% isobutane; 4% n-butane; 29% trans-2-butene; 29% 1-butene; 11% isobutylene; and 12% cis-2-butene) by inhalation for two days, 4 hr/day (Spencer *et al.*, 2001). Twenty-four hours following the final exposure, femoral bone marrow was collected to evaluate micronuclei formation in polychromatic erythrocytes. Cyclophosphamide was used as the positive control. Increases in the frequencies of micronuclei were observed in all groups treated with test material. Although a statistically significant dose

response was indicated, the difference between the low and high dose groups was minimal. Crude butadiene was positive for induction of micronuclei in this test system.

Twenty female CB6F1 mice and ten male Wistar rats were exposed to 0, 50, 200, or 500 ppm 1,3-butadiene for 5 days, 6 h/da by inhalation (Autio *et al.*, 1994). One day following exposure, smears of blood and bone marrow erythrocytes were prepared and stained. In rats, toxicity in bone marrow cells was observed in the 500 ppm exposure group. In rats, no increase in micronuclei frequencies were observed in either peripheral blood or bone marrow erythrocytes. In mice, a clear dose-dependent increase in micronuclei formation was observed in blood and bone marrow at all exposure levels tested.

Male and female Crl:CD-1 BR Swiss mice were exposed to 0; 10,780; 20,671; or 35,430 ppm butadiene concentrate (CAS # 68955-28-2: 45% 1,3-butadiene; 20% butanes; and 30% butenes) via inhalation for 2 hr/da for 2 consecutive days (Gulf Oil Chemicals Co., 1984b). Five mice per sex per dose were sacrificed on day 3 and day 4 (24 and 48 hours post-exposure), and bone marrow smears prepared. Loss of consciousness was observed in mice during exposures; no other adverse effects were observed. An increased incidence of micronuclei formation was observed at all dose levels on day three and at the two highest dose levels on day 4. Male mice exhibited an increase in micronuclei formation at the highest dose on both days.

Conclusion

Adequate data are available to evaluate the genotoxicity of crude butadiene C4. These data examine streams with a range of 1,3-butadiene content (10 to 99%). This range of 1,3-butadiene has been tested *in vitro* and *in vivo* test systems. *In vitro* studies indicate a weak mutagenic activity. *In vivo* studies demonstrate a genotoxic response from exposure to streams in this category.

4.1.6 Carcinogenicity

Inhalation

In vivo Studies in Animals

Male and female Sprague-Dawley rats were exposed to 0; 1,000; or 8,000 ppm 1,3-butadiene, 6 hr/day, 5 days/week for 111 weeks. Survival of both sexes was reduced at the high exposure level. An increase in incidence and number of animals with mammary tumors was observed in female rats at both the 1,000 and 8,000 ppm exposure levels. Increased incidences of thyroid gland adenomas and carcinomas, uterine sarcomas and Zymbal gland tumors were observed in female rats. The incidence of uterine sarcomas and Zymbal gland tumors were within the historical control range for these tumor types and may not have been related to treatment. An increased incidence in exocrine pancreas adenomas was observed in male rats at 8,000 ppm. An exposure related increase in Leydig cell tumors was observed in male rats at both concentrations.

Two cancer bioassays have been conducted in B6C3F1 mice. In the first study, male and female mice were exposed to concentrations of 0; 625; or 1,250 ppm butadiene for 61 weeks, at which time the study was canceled due to poor survivability (NTP, 1984). Numerous tumor sites were observed in both sexes. A dose-related increase in lymphomas, cardiac hemangiosarcomas and lung tumors was observed in both sexes. Increased incidence of papillomas or carcinomas of the forestomach, hepatocellular adenomas or carcinomas, ovarian granulosa cell tumors, acinar cell carcinomas of the mammary gland, brain gliomas, and Zymbal cell carcinomas were observed in one or both sexes.

Due to the poor survival rate in the initial study, a second study was conducted where B6C3F1 mice were exposed to 0, 6.25, 20, 62.5, 200 or 625 ppm 1,3-butadiene, 6 hrs/day, 5 days/week, for two years (NTP, 1993). Survival was reduced at exposure concentrations of 20 ppm and above. Tumors

were observed at numerous sites including lymphocytic lymphomas, histiocytic sarcomas, cardiac hemangiosarcomas, Harderian gland adenomas and carcinomas, hepatocellular adenomas and carcinomas, alveolar /bronchiolar adenomas and carcinomas, mammary gland adenoacanthomas and carcinomas, ovarian granulosa cell tumors and forestomach squamous cell papillomas and carcinomas. Alveolar/bronchiolar tumors were observed at the lowest dose administered in females (6.25 ppm).

Studies in Humans

Two large cohort studies provide the most definitive assessment of the relationship between cancer and butadiene exposure. One study was conducted on butadiene exposed workers in the synthetic rubber industry. Butadiene exposed workers in the butadiene monomer industry were evaluated in the second.

Delzell *et al.* (1996) evaluated mortality in a cohort of over 13,000 men employed at 8 different styrene-butadiene rubber (SBR) plants. The overall SMR for leukemia was 1.31 (95% CI = 0.97-1.74). Leukemia risks were concentrated among long-term workers with long latency working in jobs with the potential for high exposures to styrene and 1,3-butadiene. Greater than 2-fold increased leukemia risk occurred among hourly workers with more than 10 years employment and 20 years since hire and among workers in areas where there were potentially high exposures to 1,3-butadiene or styrene (e.g., polymerization, maintenance labor, laboratories). Overall about 75% of the cohort were exposed to 1,3-butadiene and 83% to styrene. In this same cohort of SBR workers, Delzell *et al.* (2001) evaluated the relationships between leukemia and exposure to 1,3-butadiene, styrene and dimethyldithiocarbamate (DMDTC). Past exposures to 1,3-butadiene, styrene and DMDTC were reconstructed through the use of exposure measurements and exposure modeling. In this analysis, leukemia mortality was significantly associated with cumulative 1,3-butadiene exposure, particularly for high ppm-years exposure levels. A stronger association was observed for cumulative 1,3-butadiene exposures with peak levels greater than 100 ppm. When concurrent exposure to styrene and DMDTC were considered, the effect of 1,3-butadiene exposure was reduced, but the exposure-response trend and apparent threshold remained. It was difficult to determine an independent effect of 1,3-butadiene exposure because of the high correlation of 1,3-butadiene exposure with styrene and DMDTC exposures. The strengths of this study are the large size, long follow-up and quantitative estimate of exposure. The weakness of this study is the concomitant exposures to styrene and DMDTC and uncertainty in the effects of 1,3-butadiene alone.

Divine and Hartman (2001) evaluated a cohort of almost 2,800 men employed at a 1,3-butadiene monomer producing plant. There were 18 cases of leukemia with an overall SMR of 1.29 (CI_{95} = 0.77 to 2.04) and all employed before 1950. The risk of leukemia decreased slightly among workers employed greater than 5 years compared to workers with less than 5-years employment in the high exposure group. This result was considered to be inconsistent with a dose-response effect. Over half the leukemia deaths occurred over 40-years since hire, which is considered an unusually long latency for leukemia. Cumulative 1,3-butadiene exposure was based on job exposure class, calendar time and length of time in job and was qualitative rather than quantitative as in the SBR study of Delzell *et al.* (2001). There was no suggestion of increasing risk with increasing 1,3-butadiene exposure. Because the exposure estimates were qualitative, it is not possible to determine the reasons for apparent absence of risk associated with 1,3-butadiene exposure in the monomer compared to the SBR study. It has been suggested that the lack of risk among monomer workers could be due to the absence of concomitant styrene and DMDTC exposures, or that 1,3-butadiene exposures were lower than the apparent threshold observed in the SBR study. The absence of risk among monomer workers is consistent with the lack of genotoxic effects among a small group of monomer workers from Prague (Albertini *et al.*, 2003). Biomarkers of exposure were related to 1,3-

butadiene exposure, but genotoxic effects were not related to 1,3-butadiene. Albertini *et al*. (2003) suggested that the lack of a genotoxic effect was not supportive of a cancer classification.

Conclusion

1,3-Butadiene is an animal carcinogen that demonstrates species differences in potency. 1,3-Butadiene is a potent, multi-site carcinogen in the mouse. Inhalation exposure to concentrations of 6.25 ppm produced lung tumors in B6C3F1 mice. Exposure to higher concentrations produced tumors at multiple sites. 1,3-Butadiene is a less potent carcinogen in rats. Although treatment related tumors were observed in the rat study, the potency and total tumor incidence was markedly different when compared to the mouse bioassays. The differences observed are likely due to the difference in 1,3-butadiene metabolism described in section 4.1.1.

Carcinogenic effects of 1,3-butadiene are more difficult to discern for humans. Epidemiology studies of workers exposed to 1,3-butadiene in the monomer industry demonstrated no increase in carcinogenic risk. In the synthetic rubber industry workers exposed to 1,3-butadiene demonstrated an increased risk of leukemia associated with long term exposure to high levels of 1,3-butadiene. The association was stronger when co-exposures to styrene and DMDTC were also considered. The difference in leukemia risk between these two groups could be related to differences in exposure to 1,3-butadiene, or the need for co-exposure to other agents in addition to 1,3-butadiene (styrene, DMDTC) for the expression of leukemia.

4.1.7 Toxicity for Reproduction

Several studies evaluated the reproductive and developmental toxicity of streams in the Crude Butadiene C4 Category (Tables 10 and 11). The streams evaluated ranged in 1,3-butadiene content from 10 to 100%. The majority of studies were conducted under standard protocols in compliance with GLP (good laboratory practices).

Table 10. Summary of Reproductive Toxicity Data

CAS RN and Stream Name (% 1,3-Butadiene)	Test Organism	OECD Test Guideline	NOAEL (mg/m^3)
68476-52-8 C4 Crude Butadiene (10)	Crl:CD Rat	422	>20,000 (Systemic) >20,000 (Reproductive)
106-99-0 1,3-Butadiene (>99)	Crl:CD Rat	421	>663 (Systemic) >13,260 (Reproductive)

Table 11. Summary of Developmental Toxicity Data

CAS RN and Stream Name (% 1,3-Butadiene)	Test Organism	OECD Test Guideline	NOAEL (mg/m^3)
68476-52-8 C4 Crude Butadiene (10)	Crl:CD Rat	422	>20,000 (Developmental) >20,000 (Maternal)
106-99-0 1,3-Butadiene (>99)	Crl:CD Rat	421	>13,260 (Developmental) >663 (Maternal)
106-99-0 1,3-Butadiene (>99)	CD Rat	414	>2,210 (Developmental) >442 (Maternal)
106-99-0 1,3-Butadiene (>99)	CD-1 Swiss Mice	414	>88.4 (Developmental) >88.4 (Maternal)

Effects on Fertility

Studies in Animals

Reproductive toxicity of C4 crude butadiene (CAS # 68476-52-8: 10% 1,3-butadiene; 4% isobutane; 4% n-butane; 29% trans-2-butene; 29% 1-butene; 11% isobutylene; and 12% cis-2-butene) was evaluated in an OECD 422 Repeat Dose Reproductive/Developmental Toxicity Screen (Carney *et al.*, 2001). Groups of 12 adult male and female Crl:CD Sprague-Dawley rats were exposed via inhalation to crude butadiene at concentrations of 0; 2,000; 10,000; or 20,000 mg/m^3, 6 hr/day, 7 days per week two weeks prior to breeding, during breeding, continuing to gestation day 19. Male rats were exposed for 36 to 37 days. No differences were observed in parental body weights, body weight gains or feed consumption between the groups. No treatment related effects were observed on mating, conception, fertility, or time to mating. Evaluations of gonadal function revealed no difference between treated and control groups. The NOAEL for reproductive toxicity was determined to be 20,000 mg/m^3.

Reproductive toxicity of 1,3-butadiene was evaluated in an OECD 421 inhalation reproduction and developmental toxicity screening test (WIL Research Laboratories, 2003). Adult male and female Crl:CD rats were exposed to concentrations of 0; 663; 3,313; or 13,260 mg/m^3 1,3-butadiene two week prior to breeding, during mating, gestation and lactation for a total of 83 to 84 consecutive days for F0 males, 60 to 70 total days for F0 females and 7 consecutive days for 2 groups of F1 offspring (one male and one female per litter on post natal days 21 to 27 or 28 to 34). In F0 and F1 animals a reduction in body weight was observed at 3,313 and 13,260 mg/m^3. Clinical signs of toxicity, chromodacryorrhea, chromorhinorrhea, and salivation in F0 animals as well as dried red material in the perioral and perinasal regions in the F1 pups were observed at 13,260 mg/m^3. No effect at any dose level was observed in any reproductive parameter examined including gonadal function, mating behavior, conception, gestation, parturition, and lactation. The systemic NOAEL for this study was 663 mg/m^3. The reproductive NOAEL was >13,260 mg/m^3.

The effect of 1,3-butadiene exposure on fertility in male mice was examined in a rodent dominant lethal test and sperm-head morphology assay (Morrissey, 1990). Male mice were exposed to 0; 442; 2,210; or 11,040 mg/m^3 1,3-butadiene via inhalation for 5 days, 6 hr/day. In the dominant lethal assay, CD-1 male mice were then mated to two unexposed female mice/week for eight consecutive weeks. In the two low dose groups slight differences were observed in ratio of dead to total implants, percentage of females with ≥2 dead implants and number of dead implants per pregnancy (also observed in the high dose group during week 1). No differences were observed in number of

pregnant females, implantations per litter, number of live fetuses, dead implantations/total implantations, or number of resorptions during weeks 1 and 2. No differences were observed for any endpoint during weeks 3 to 8. It was concluded, despite the lack of dose response, that 1,3-butadiene had an effect on mature germ cells. To assess sperm morphology, B6C3F1 mice were used and maintained for five weeks post exposure (Morrissey, 1990). At the end of the post exposure period, the reproductive tract was evaluated for gross lesions and sperm were obtained from the right cauda epididymus. A dose dependent increase in percentage of abnormal sperm was observed, becoming significantly different from control at the two highest exposure concentrations.

Developmental Toxicity

As part of an OECD 422 Repeat Dose Reproductive/Developmental Toxicity Screen (Carney *et al.*, 2001), no developmental toxicity was observed in Crl:CD Sprague-Dawley rats following exposure to C4 crude butadiene (CAS # 68476-52-8: 10% 1,3-butadiene; 4% isobutane; 4% n-butane; 29% trans-2-butene; 29% 1-butene; 11% isobutylene; and 12% cis-2-butene). Groups of 12 adult male and female rats were exposed via inhalation to crude butadiene at concentrations of 2, 10, or 20 mg/L (2,000; 10,000; or 20,000 mg/m^3), 6 hr/day, 7 days per week, 2 weeks prior to breeding, during breeding, and continuing to gestation day 19. No treatment related effects were observed in paternal body weights, body weight gains or feed consumption during the study. No difference was observed in number of viable litters, gestation length, litter size, pre implantation loss, pup body weight, or pup sex ratio. An increase was observed in post implantation loss in the low exposure group. This observation was considered spurious, given the lack of dose response. A single pup in the high dose group exhibited a hernia. This finding was considered spurious due to its low incidence. The NOAEL for this study was 20,000 mg/m^3.

A guideline OECD 414 developmental toxicity study was conducted in pregnant CD rats exposed to 0; 40; 200; or 1,000 ppm 1,3-butadiene on gestation days 6 to 15, 6 hr/day (Morrissey, 1990). Dams were sacrificed on gestation day 20. Decreased weight gain was observed in dams at 2,210 mg/m^3. There were no significant differences among the groups for number of live fetuses per litter, percent resorptions, malformations per litter, placental or fetal body weights or sex ratio. There was no evidence of developmental toxicity in any of the treated groups. The maternal NOAEL for this study was 442 mg/m^3 and the fetal NOAEL was 2,210 mg/m^3.

Developmental toxicity was evaluated in Crl:CD rats exposed to 0; 663; 3,313; or 13,260 mg/m^3 (0; 301; 1,507; or 6,006 ppm, respectively) 1,3-butadiene during the conduct of an OECD 421 inhalation reproduction and developmental toxicity screening test (WIL Research Laboratories, 2003). Adult male and female Crl:CD rats were exposed to 1,3-butadiene two week prior to breeding, during mating, gestation and lactation for a total of 83 to 84 consecutive days for F0 males, 60 to 70 total days for F0 females and 7 consecutive days for two groups of F1 offspring (one male and one female per litter on post natal days 21 to 27 or 28 to 34). In F1 offspring, a reduction in weight gain was observed in the 3,313 and 13,260 mg/m^3 groups during later stages of the lactation period. No indications of fetal toxicity or teratogenicity were observed. The systemic NOAEL for F0 and F1 animals was 663 mg/m^3. The developmental NOAEL was 13,260 mg/m^3.

Pregnant female CD-1 mice were exposed via inhalation to 0; 88.4; 442; or 2,210 mg/m^3 (0; 40; 200; or 1,000 ppm, respectively) 1,3-butadiene on day 6 to 15 of gestation, 6 hr/day using the OECD 414 developmental toxicity guideline (Morrissey, 1990). On day 18 of gestation, dams were sacrificed and maternal and fetal evaluations were made. Decreased maternal body weight gain was observed at 442 and 2,210 mg/m^3. Male and female fetal weights were reduced in the high dose groups. Placental weights were reduced for male fetuses at 200 ppm and males and females at 2,210 mg/m^3. Fetal variations (supernumary ribs and reduced sternebrae ossification) were increased in the 442 and 2,210 mg/m^3 groups. The maternal and developmental NOAEL for this study was 88.4 mg/m^3.

Conclusion

Effects on fertility and developmental toxicity of C4 Crude Butadiene (high butadiene concentration) are adequately defined with the available data. A stream with 1,3-butadiene concentration of approximately 10% produced no reproductive or developmental toxicity in rats exposed to concentrations as high as 20,000 mg/m^3. No reproductive or developmental toxicity was observed in rats exposed to concentrations up to 13,260 mg/m^3 1,3-butadiene. No developmental toxicity was observed in rats exposed to 2,210 mg/m^3 1,3-butadiene in the presence of maternal toxicity. These two streams cover the range of C4 Crude Butadiene streams (10% to approximately 100% 1,3-butadiene). As observed with other endpoints, mice are more susceptible than rats to developmental and reproductive toxicity of 1,3-butadiene, most likely due to an increased metabolic capacity in mice to form reactive metabolites. This is evident by the observation of developmental toxicity in mice at 442 mg/m^3 1,3-butadiene exposure. There is some indication of male mediated toxicity in mice following 1,3-butadiene exposure; however, the effect appears to be weak. As humans metabolize 1,3-butadiene in a manner more consistent with rats than mice, reproductive and developmental toxicity data developed in rats is more appropriate to use in assessing human risk.

The ability of 1,3-butadiene to cause ovarian atrophy is dependent on the production of the diepoxide metabolite and this differs between species (U.S. EPA, 2002). The mouse is the most sensitive species in terms of ovarian atrophy induction following 1,3-butadiene exposure while the rat is resistant to this effect. The observed species differences correlate with the production of the diepoxide metabolite of 1,3-butadiene, with the mouse producing higher levels of this toxic intermediate. Direct administration of the diepoxide metabolite of 1,3-butadiene can affect the rat ovary, albeit at higher dose levels than required for inducing similar effects in mice. Therefore, the mouse ovary is more sensitive to the toxic effects of both 1,3-butadiene and the diepoxide metabolite (U.S. EPA, 2002). Species differences in metabolism are explained in Section 4.1.1.

4.2 Assessment Summary for Human Health

Crude Butadiene C4 streams have a low order of acute toxicity. The components of Crude Butadiene C4 streams are gaseous at normal temperature and pressure; thus, ingestion or dermal absorption of this material is unlikely. Minimal effects were observed at concentrations of 5,300 mg/m^3.

Liquid Crude Butadiene C4 (test material was cooled in a dry ice bath) did not produce dermal or ocular irritation in rabbits. Exposure to liquid Crude Butadiene C4 is unlikely, as the components of the streams in this category are gases at normal temperature and pressure.

A species difference in repeated dose toxicity of Crude Butadiene C4 was apparent between rats and mice. Minimal effects were reported in rat repeated dose toxicity tests exposed to several Crude Butadiene C4 streams (1,3-butadiene content ranging from 10 to 99.2%). The no observable adverse effect levels were the highest concentrations tested or 17,679; 20,000; or 25,100 mg/m^3 (8,000; 9,060; or 11,365 ppm, respectively) following 90, 36, or 9 days or exposure, respectively. In contrast, mortality was observed in mice exposed to 2,761 mg/m^3 1,3-butadiene (99.2%) for 90 days. Well-documented species differences in 1,3-butadiene metabolism are the likely reason for the noted differences in repeat dose toxicity. Mice produce greater amounts of toxic metabolites following 1,3-butadiene exposure than rats. The existing metabolism data suggest that metabolism in humans appears to be more like metabolism in rats than in mice.

Test data demonstrate that Crude Butadiene C4 can produce genotoxicity. *In vitro*, Crude Butadiene C4 demonstrated little activity in reverse mutation assays conducted in *Salmonella typhimurium* either in the presence or absence of metabolic activation. In addition, Crude Butadiene C4 did not increase the number of transformed foci in C3H/10T1/2 clone 8 mouse embryo fibroblast cells. In the mouse lymphoma assay, evidence of mutagenic activity in mouse lymphoma L5178Y cells in

culture was observed in the absence of metabolic activation, but not in the presence of metabolic activation. *In vivo*, several Crude Butadiene C4 streams, containing 10 to 45% 1,3-butadiene, induced micronuclei formation in rats and mice following inhalation exposure.

Cancer data exist for 1,3-butadiene and these data are used as a surrogate for the Crude Butadiene C4 Category. Species differences exist in the carcinogenic response to 1,3-butadiene exposure. Similar to repeat dose data, mice are more sensitive than rats. Tumors are observed at lower exposure concentrations and at greater incidence than rats. In humans, an association between leukemia incidence and 1,3-butadiene exposure was observed in synthetic rubber workers exposed to 1,3-butadiene. The association was stronger when co-exposures to styrene and DMDTC were considered. No increase in leukemia incidence was observed in butadiene monomer workers.

No reproductive or developmental toxicity was observed in rats exposed to Crude Butadiene C4 during the conduct of an OECD 422 repeat dose reproductive/developmental toxicity screen. Exposures to concentrations of 20,000 mg/m^3 were without effect. Further, in a prenatal developmental toxicity study, inhalation exposure of pregnant rats to 1,3-butadiene on days 5 to 16 (inclusive) of gestation elicited no developmental toxicity at any tested concentration up to 2,210 mg/m^3. Maternal toxicity was observed at levels of 442 mg/m^3. Similar to observations of species differences in repeat dose toxicity, mice were more sensitive than rats in developmental and reproductive toxicity following exposure to 1,3-butadiene. This increased sensitivity was apparent in effects on male germ cells observed in a dominant lethal study and an assessment of sperm morphology in male mice and fetal effects observed in a prenatal developmental toxicity study. Chronic exposure to 1,3-butadiene increased the incidence of ovarian atrophy in mice, most likely related to the formation of butadiene diepoxide.

5 HAZARDS TO THE ENVIRONMENT

5.1 Aquatic Toxicity

The aquatic toxicity of streams in this category is expected to fall within a relatively narrow range regardless of their composition. This is expected because the constituent chemicals of these streams are neutral organic hydrocarbons whose toxic mode of action is non-polar narcosis (Ramos *et al.*, 1998). The toxic mechanism of short-term toxicity for these chemicals is disruption of biological membrane function (Van Wezel, 1995), and the differences between toxicities (i.e., LC/LL_{50}, EC/EL_{50}) can be explained by the differences between the target tissue-partitioning behavior of individual constituent chemicals (Verbruggen *et al.*, 2000).

The existing fish toxicity database for hydrophobic, neutral organic chemicals, which comprise the streams in this category, supports a critical body residue (CBR) for these chemicals between approximately 2-8 mmol/kg fish (wet weight) (McCarty *et al.*, 1991; McCarty and Mackay, 1993). The CBR is the internal concentration of a toxicant that causes mortality. When normalized to lipid content for most organisms, the CBR is approximately 50 µmol/g of lipid (Di Toro, 2000). Therefore, only hydrocarbon streams with components of sufficient water solubility, such that their molar sum in solution is high enough to produce a total partitioning to the organism of approximately 50 µmol of hydrocarbon per gram of lipid will demonstrate lethality.

Measured data are not available for the aquatic toxicity endpoints. However, structure-activity relationship (SAR) data developed with the ECOSAR model (Cash and Nabholz, 1999) were used to assess the aquatic toxicity for three trophic levels [the ECOSAR model used was from EPIWIN (1999)]. The ECOSAR model is a reliable and valid SAR model to apply to constituent chemicals from this category because it is based on a related chemical dataset that calculates the toxicity of neutral organic hydrocarbons whose toxic mode of action is non-polar narcosis. The calculated

aquatic toxicity values were determined using measured log P_{ow} values (ECOSAR requires selected physicochemical data and chemical structure to calculate effect concentrations).

Calculated aquatic toxicity values for chemicals representative of category members fall within a relatively narrow range. The effect range is a function of the range of log P_{ow} values identified for the chemicals. Streams in this category are expected to demonstrate 96-hour LC_{50} fish toxicity values in the range of 6.28 to 40.98 mg/L, 48-hour LC_{50} invertebrate toxicity values in the range of 7.15 to 43.88 mg/L, and 96-hour EC_{50} alga toxicity values in the range of 4.71 to 27.42 mg/L (Table 12).

Table 12. Summary of Aquatic Toxicity Data for Chemical Constituents in the Crude Butadiene C4 Category

Chemical Constituent (Log P_{ow}*)	Fish Toxicity 96-hour LC_{50} (mg/L)	Invertebrate Toxicity 48-hour EC_{50} (mg/L)	Alga Toxicity 96-hour EC_{50} (mg/L)
Isobutane (2.76)	8.32	9.39	6.13
n-Butane (2.89)	6.28	7.15	4.71
Isobutylene (2.34)	19.93	21.86	13.94
cis-Butene-2 (2.31)	21.26	23.28	14.81
trans-Butene-2 (2.33)	20.36	22.32	14.22
Butene-1 (2.40)	17.50	19.28	12.33
1,3-Butadiene (1.99)	40.98	43.88	27.42

* The log P_{ow} values used in the ECOSAR model are from the EPIWIN experimental database.

5.2 Assessment Summary for the Environment

Results of distribution modeling show that streams in the Crude Butadiene C4 Category will partition primarily to the air compartment, with a negligible amount partitioning to water. Although constituents have a moderate degree of water solubility, wet deposition of category constituents is not likely to play a significant role in their atmospheric fate because they rapidly photodegrade. Volatilization to the air will contribute to the rapid loss of category constituents from aqueous and terrestrial habitats. In the air, these constituents have the potential to rapidly degrade through indirect photolytic processes mediated primarily by hydroxyl radicals with calculated degradation half-lives ranging from 1.9 to 52.6 hours, depending on hydroxyl radical concentration. Aqueous photolysis and hydrolysis will not contribute to the transformation of category constituents in aquatic environments because they are either poorly or not susceptible to these reactions.

Although the biodegradability of streams in this category has not been evaluated with standard testing procedures because of their high volatility, studies have demonstrated that several category constituents can be degraded by bacteria isolated from soil and surface water samples. The results from these studies suggest that streams from this category are subject to microbial degradation. However, biodegradation is unlikely to contribute to the overall degradation of these streams because they tend to partition to the air compartment due to high volatility at ambient temperatures, and thus are less likely to be available to degrading microorganisms.

Due to the fact that streams in this category are gaseous at ambient temperature and pressure and expected to partition predominantly to the atmosphere, no aquatic toxicity testing was conducted. However, the ECOSAR model was used to predict aquatic toxicity using the equation for neutral organics, a reliable estimation method for this class of chemicals. Calculated acute toxicity values of selected category constituents for fish (96-hr) and invertebrates (48-hr) range from 6.28 to 40.98

mg/L and from 7.15 to 43.88 mg/L, respectively. For algae, the calculated 96-hr EC_{50} ranges from 4.71 to 27.42 mg/L.

6 DATA SUMMARY

Physico-chemical, environmental fate and effects, and human health data that characterize the two streams in the Crude Butadiene C4 Category are summarized in Tables 13 and 14. CAS RNs are associated with streams as follows:

- **C4 Crude Butadiene Stream**
  - 68476-52-8
  - 68187-60-0
  - 68955-28-2
  - 64742-83-2
  - 68476-44-8
  - 68956-54-7
  - 68477-41-8
  - 25167-67-3
- **Butadiene Unit Heavy Ends Stream**
  - 69103-05-5
  - 68477-41-8
  - 68512-91-4

Table 13. Physico-Chemical and Environmental Data Used to Characterize Streams and CAS RNs in the Crude Butadiene C4 Category (ranges are based on data for the most representative chemical subset for category streams and CAS RNs)

Endpoint	Crude Butadiene C4 Category Streams and CAS RNs								
							Butadiene Unit Heavy Ends Stream		
	C4 Crude Butadiene Stream								
	68955-28-2	68476-44-8	25167-67-3	68187-60-0	68476-52-8	68956-54-7	68477-41-8	68512-91-4	69103-05-5
Melting Point*/ Range (°C)	-145.0 to -105.5 (m)								
Boiling Point*/ Range (°C)	-11.7 to 0.8 (m)								
Vapor Pressure*/ Range (hPa)	2.33 E3 to 3.08 E3 (m)								
Log P_{ow}*/ Range	1.99 to 2.89 (m)								
Water Solubility*/ Range (mg/L)	135.6 to 792.3 (m)								
Direct Photodegradation	Direct photolysis will not contribute to degradation								
Indirect (OH-) Photodegradation* (half-life, hrs) (c)	1.9 to 52.6 (a)								
Hydrolysis	Hydrolysis will not contribute to degradation								
Distribution*	>99.9% partitions to air <0.1% partitions to water								
Biodegradation	Potential to biodegrade								
96-hr Fish Acute Toxicity* (mg/L)	22.03 to 37.59 (c)								
48-hr Invert Acute Toxicity* (mg/L)	24.11 to 40.27 (c)								
96-hr Alga Toxicity* (mg/L)	15.35 to 25.27 (c)								

* Constituent chemicals used to define selected endpoints include: isobutane; n-butane; isobutylene; cis-butene-2; trans-butene-2; butene-1; 1,3-butadiene
(m) Measured values (c) Calculated values (a) Atmospheric half-life values are based on a 12-hr day.

Table 14. Human Health Data Summary Used to Characterize Streams and CAS RNs in the Crude Butadiene C4 Category

Endpoint	Human Health Data Based on 1,3-Butadiene Content (wt%) for Crude Butadiene C4 Category Streams (CAS RNs)									
	10%	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**
	C4 Crude Butadiene Stream (64742-83-2, 68955-28-2, 68476-44-8, 25167-67-3, 68187-60-0, 68476-52-8, 68956-54-7, 68477-41-8)									
	Butadiene Unit Heavy Ends Stream (68477-41-8, 68512-91-4, 69103-05-5)									
Acute Toxicity (rat)	LC50 >5,300 mg/m^3									LC50 =285,000 mg/m^3
Irritation						Non Irritating (eyes / skin)				
Repeat Dose Toxicity (rat)	NOAEL >20,000 mg/m^3			NOAEL >25,100 mg/m^3						NOAEL >17,679 mg/m^3
Mutagenicity Ames Assay						Negative				Weakly Positive
Mutagenicity Mouse Micronucleus	Positive			Positive						Positive
Reproductive Toxicity (rat)	NOAEL >20,000 mg/m^3									NOAEL >13,260 mg/m^3
Developmental Toxicity (rat)	NOAEL (M&F) >20,000 mg/m^3									NOAEL (M) >663 mg/m^3 NOAEL (F) >13,260 mg/m^3

M Male F Female

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APPENDIX I

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 hydrocarbon streams 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., C2, C3, C4, etc. Propane and propylene are examples of C3 hydrocarbons and benzene, hexene, and cyclohexane are a few examples of the C6 hydrocarbons.

2. Refinery Gas Separation

Ethylene and propylene are also produced by separation of these olefins 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. Crude Butadiene C4 Streams from the Ethylene Process

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 (C2+). 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 pressure systems. (See Figure 4 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. It is a subset of these mixed streams that make up streams in the Crude Butadiene C4 Category.

C. Crude Butadiene C4 Category Streams

1. C4 Crude Butadiene

The C4 Crude Butadiene stream (previously referred to as Butadiene Concentrate stream) is separated by distillation from the condensed portion of the cracked gas. Typically, C4 Crude Butadiene is a fairly narrow boiling range mixture consisting predominately of C4 hydrocarbons. C4 Crude Butadiene may also contain lesser amounts of C3 or lighter hydrocarbons and C5 and heavier hydrocarbons, because the separation technology is not perfect. The 1,3-butadiene content of these streams is typically 40 to 60%, but can range from approximately 10 to 82% (Table 2). C4 Crude Butadiene streams are sometimes produced in "on purpose" butadiene units using, for example, an oxydehydrogenation process.

2. Butadiene Unit Heavy Ends

Several different technologies are used to separate 1,3-butadiene from the C4 Crude Butadiene stream produced by the ethylene process. All of these technologies use a solvent to effect the separation.

In one technology, the C4 Crude Butadiene stream is fed to an extractive distillation (ED) column and a C4 mixture referred to as “raffinate” (i.e., C4 olefins and paraffins) is separated from the top of the distillate column. The bottom from the ED column consists of solvent rich in 1,3-butadiene and small amounts of other C4s. The rich solvent is fed to the solvent stripper where the 1,3-butadiene and other C4s are taken overhead (removed). The stripped, lean solvent is transferred from the bottom of the stripper back to the ED tower. The overhead of the stripper is condensed and fed to the rerun tower (or postfractionator) where high purity 1,3-butadiene is produced as the overhead. Bottoms of the rerun tower consist of the higher boiling constituents of C4 Crude Butadiene stream (e.g., 1,2-butadiene). The 1,3-butadiene content of streams in the Butadiene Unit Heavy Ends stream (previously referred to as High Butadiene Heavy Ends) covered by this test plan can range from 13 to 92% (Table 2).

3. Pyrolysis C3+ and Pyrolysis C4+

Butadiene concentrate sometimes consists of the entire C3+ or C4+ portion of the cracked gas stream (Pyrolysis C3+ and C4+ streams, previously referred to as Full Range Butadiene Concentrate stream). In this case, the carbon number distribution is between C3 and C12 or even higher. Normally the C4+ full-range 1,3-butadiene concentrate is split by distillation into two streams, a C4 Crude Butadiene stream, described above, and pyrolysis gasoline stream. The 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 (Table 15). There are only two examples where these broad-range streams have been reported to have been isolated. In both cases, it was a result of a shutdown of process equipment and not the result of routine production conditions. The Pyrolysis C4+ stream was site limited and the Pyrolysis C3+ was not. The 1,3-butadiene content of Pyrolysis C3+ and Pyrolysis C4+ streams can range from 12 to 42% (Table 2). The Pyrolysis C3+ and Pyrolysis C4+ streams are discussed as a separate category.

4. 1,3-Butadiene

High purity 1,3-butadiene (99.5%+) is produced by separation from C4 crude butadiene produced by the ethylene process. This separation is accomplished by using a solvent process, either extraction or more typically extractive distillation. “On purpose” units also produce a small percentage of the commercially available 1,3-butadiene by dehydrogenation and subsequent separation.

Figure 5. Crude Butadiene C4 Process Streams Flow Diagram from the Ethylene Manufacturing Process Unit

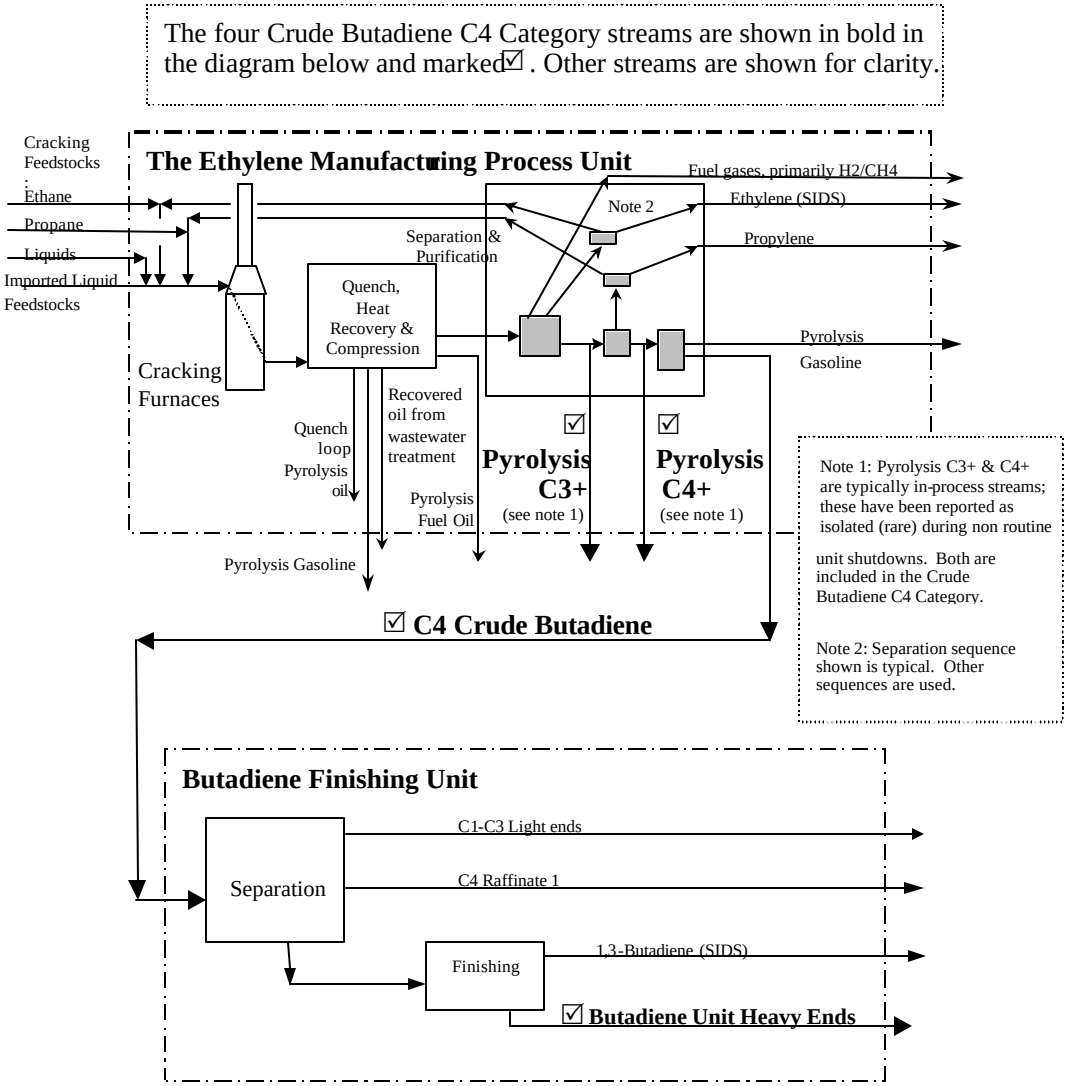


Table 15. HPV Program Categories Sponsored by the Olefins Panel of the American Chemistry Council

Category Number	Category Name
1	Crude Butadiene C4
2	Low 1,3-Butadiene C4
3	C5 Non-Cyclics
4	Propylene Streams
5	High Benzene Naphthas
6	Low Benzene Naphthas
7,8,9	Resin Oils & Cyclodiene Dimer Concentrates
10	Fuel Oils
11	Pyrolysis C3+ and Pyrolysis C4+

APPENDIX II

ROBUST SUMMARIES OF STUDIES USED TO CHARACTERIZE THE CRUDE BUTADIENE C4 CATEGORY

PHYSICO-CHEMICAL ROBUST SUMMARIES

Melting Point

Test Substance*:	Other TS
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Melting Point estimations performed by MPBPWIN are based on the average result of the calculation methods of K. Joback and Gold and Ogle. Joback's Method is described in Joback, K.G. 1982. A Unified Approach to Physical Property Estimation Using Multivariate Statistical Techniques. In The Properties of Gases and Liquids. Fourth Edition. 1987. R.C. Reid, J.M. Prausnitz and B.E. Poling, Eds. The Gold and Ogle Method simply uses the formula Tm = 0.5839Tb, where Tm is the melting point in Kelvin and Tb is the boiling point in Kelvin.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical — Calculated MP (°C) — Measured* MP (°C) Isobutane: -132.55 / -138.3 n-butane: -120.28 / -138.2 isobutylene: -130.88 / -140.4 cis-butene-2: -120.41 / -105.5 trans-butene-2: -120.41 / -105.5 butene-1: -121.74 / -145.0 1,3-butadiene: -123.21 / -108.9 * Experimental values are supplied by the MPBPWIN program database (EXP_MBVP.DB) which contains more than 11,000 organic compounds with reliably measured

	values which are taken from SRC's PHYSPROP Database. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the melting range of this category are C4 hydrocarbons that are common across the 10 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated values, products in this category can have a melting range of -132.55 to -120.28 °C. Based on the measured values, products in this category can have a melting range of -145.0 to -105.5°C.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the

	MPBPWIN program and represent a potential melting range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. WSKOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "melting point". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Boiling Point

Test Substance*:	Other TS
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Pressure:	760 mm Hg
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Boiling Point estimations performed by MPBPWIN are based on the calculation method of S. Stein and R. Brown in "Estimation of Normal Boiling Points from Group Contributions". 1994. J. Chem. Inf. Comput. Sci. **34**: 581-587.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated BP (°C) / Measured* BP (°C) Isobutane 3.21 -11.7 n-butane 19.58 -0.5 isobutylene 10.18 -6.9 cis-butene-2 27.82 0.8 trans-butene-2 27.82 0.8 butene-1 17.57 -1.3 1,3-butadiene 15.55 -4.4 * Experimental values are supplied by the MPBPWIN program database (EXP_MBVP.DB) which contains more than 11,000 organic compounds with reliably measured values which are taken from SRC's PHYSPROP Database. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the boiling range of this category are C4 hydrocarbons that are common across the 10 CAS numbers. Crude butadiene category

	products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated values, products in this category can have a boiling range of 3.21 to 27.82 °C. Based on the measured values, products in this category can have a boiling range of -11.7 to 0.8°C.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the MPBPWIN program and represent a potential boiling point range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. WSKOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "boiling point". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext
IUCLID fields include:
- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Vapor Pressure

Test Substance*:	Other TS
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Vapor Pressure estimations performed by MPBPWIN are based on the average result of the calculation methods of Antoine and Grain. Both methods use boiling point for the calculation. The Antoine Method is described in the Handbook of Chemical Property Estimation. Chapter 14. W.J. Lyman, W.F. Reehl and D.H. Rosenblatt, Eds. Washington, D.C.: American Chemical Society. 1990. A modified Grain Method is described on page 31 of Neely and Blau's Environmental Exposure from Chemicals, Volume 1, CRC Press. 1985.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated VP (hPa) / Measured* VP (hPa) Isobutane: 3.45 E3 / 3.08 E3 n-butane: 2.41 E3 / 2.43 E3 isobutylene: 2.97 E3 / 3.08 E3 cis-butene-2: 2.31 E3 / 2.33 E3 trans-butene-2: 2.31 E3 / 2.33 E3 butene-1: 2.48 E3 / 3.00 E3 1,3-butadiene: 2.73 E3 / 2.81 E3 * Experimental values are supplied by the MPBPWIN program database (EXP_MBVP.DB) which contains more than 11,000 organic compounds with reliably measured values which are taken from SRC's PHYSPROP Database. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is

	why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the vapor pressure range of this category are C4 hydrocarbons that are common across the 10 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated values, products in this category can have a vapor pressure range of 2.31 E^3 to 3.45 E^3 hPa. Based on the measured values, products in this category can have a vapor pressure range of 2. 33 E^3 to 3.08 E^3 hPa.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the MPBPWIN program and represent a potential vapor pressure range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. MPBPWIN is contained in the computer program EPIWIN. 1999. Estimation Program

	Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "vapor pressure". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Partition Coefficient

Test Substance*:	Other TS
Method/Guideline:	Calculated values using KOWWIN version 1.65, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Octanol / Water Partition Coefficient estimations performed by KOWWIN are based on an atom/fragment contribution method of W. Meylan and P. Howard in "Atom/fragment contribution method for estimating octanol-water partition coefficients". 1995. *J. Pharm. Sci*. **84**:83-92.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated log K_{ow} / Measured* log K_{ow} Isobutane 2.23 2.76 n-butane 2.31 2.89 isobutylene 2.23 2.34 cis-butene-2 2.09 2.31 trans-butene-2 2.09 2.33 butene-1 2.17 2.40 1,3-butadiene 2.03 1.99 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the partition coefficient range of this category are C4 hydrocarbons that are common across the 10 CAS numbers. Crude butadiene

	category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated K_{ow} values, products in this category can have a partition coefficient range of 2.03 to 2.31. Based on the measured K_{ow} values, products in this category can have a partition coefficient range of 1.99 to 2.89.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the KOWWIN program and represent a potential partition coefficient range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "partition coefficient". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext
IUCLID fields include:
- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Water Solubility

Test Substance*:	Other TS
Method/Guideline:	Calculated values using WSKOWWIN version 1.36, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Water Solubility estimations performed by WSKOWWIN are based on a Kow correlation method described by W. Meylan, P. Howard and R. Boethling in "Improved method for estimating water solubility from octanol/water partition coefficient". *Environ. Toxicol. Chem*. **15**:100-106. 1995.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol o r guideline, analytical method.**	Chemical / Calculated WS (mg/L) / Measured* WS (mg/L) Isobutane 496.4 175.1 n-butane 424.1 135.6 isobutylene 495.6 399.2 cis-butene-2 652.7 423.5 trans-butene-2 652.7 407.1 butene-1 557.7 354.8 1,3-butadiene 732.4 792.3 * Experimental K_{ow} values supplied by the WSKOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the water solubility range of this category are C4 hydrocarbons that are common across the 10 CAS numbers. Crude butadiene

	category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated K_{ow} values, products in this category can have a water solubility range of 424.1 to 732.4 mg/L. Based on the measured K_{ow} values, products in this category can have a water solubility range of 135.6 to 792.3 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include values estimated using calculated K_{ow} and experimental K_{ow} values available in the WSKOWWIN program and represent a potential water solubility range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. WSKOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "water solubility". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext
IUCLID fields include:
- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

ENVIRONMENTAL FATE ROBUST SUMMARIES

Photodegradation (Direct)

Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Type (air, soil, water, other):	Not applicable
Light Source: **Light Spectrum:** • **Wave length value (upper/lower)**	Not applicable Not applicable
Relative Intensity:	Not applicable
Test Substance Spectrum:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol**	Not applicable
Direct Photolysis:** **Results: half-life, % degradation, quantum yield**	**Summary** In the environment, photolysis will not significantly contribute to the degradation of chemicals in the Crude Butadiene C4 Category (C4 refers to a chemical with 4 carbons). The Crude Butadiene C4 Category includes two process streams: • **C4 Crude Butadiene** • **Butadiene Unit Heavy Ends** Ten CAS numbers (see Test Substance) identify products derived from these process streams. As discussed below, the reaction process involved in direct photolysis occurs when sufficient light energy excites a molecule to the degree that a structural transformation occurs. In general, products in this

	category do not contain component chemicals that will undergo direct photolysis. **The Crude Butadiene C4 Category** A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. Process streams containing 10 to 92% butadiene are referred to as "crude butadiene." The CAS numbers or streams in this category consist of complex mixtures of hydrocarbons. Most commercial products in this category have a carbon number distribution predominantly between C3 and C5. All of these streams contain significant levels of 1,3-butadiene and olefins, which is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Crude Butadiene C4. The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process). Crude butadiene streams arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the two process streams in this category are: • **C4 Crude Butadiene** is produced by the distillation of a condensed portion of cracked gas in an ethylene process. C4 Crude Butadiene typically contains 40% to about 60% 1,3-butadiene, but could contain between 10% and 82% butadiene. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. • **Butadiene Unit Heavy Ends** is produced by extractive distillation of cracked gas. The 1,3-butadiene content of this mixed stream ranges from 13% to 92%. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. Only three companies report isolating this stream which is more typically an un-isolated intermediate.

	Photolysis of Hydrocarbons The direct photolysis of an organic molecule occurs when it absorbs sufficient light energy to result in a structural transformation (2). The reaction process is initiated when light energy in a specific wavelength range elevates a molecule to an electronically excited state. However, the excited state is competitive with various deactivation processes that can result in the return of the molecule to a non excited state. The absorption of light in the ultra violet (UV)-visible range, 110-750 nm, can result in the electronic excitation of an organic molecule. Light in this range contains energy of the same order of magnitude as covalent bond dissociation energies (2). Higher wavelengths (e.g., infrared) result only in vibrational and rotational transitions, which do not tend to produce structural changes to a molecule. The stratospheric ozone layer prevents UV light of less than 290 nm from reaching the earth's surface. Therefore, only light at wavelengths between 290 and 750 nm can result in photochemical transformations in the environment (2). Although the absorption of UV light in the 290-750 nm range is necessary, it is not always sufficient for a chemical to undergo photochemical degradation. Energy may be re-emitted from an excited molecule by mechanisms other than chemical transformation, resulting in no change to the parent molecule. A conservative approach to estimating a photochemical degradation rate is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by the molecule (3). Saturated hydrocarbons do not absorb light above 200 nm. Some characteristic absorbance maxima (λ_{max}) and associated molar absorptivities (ε) for selected unsaturated hydrocarbons are shown below (2):

		l **below 290 nm**	
	Hydrocarbon	λ_{max}	e
	Ethylene	193	10,000
	1,3-Butadiene	217	2,090
Direct Photolysis: (cont.)** **Results: half-life, % degradation, quantum yield**	Olefins with one double bond, two conjugated double bonds, or multiple un-conjugated bonds, which constitute the majority of the chemicals in the Crude Butadiene C4 Category, do not absorb appreciable light energy above 290 nm. The absorption of UV light to cause cis-trans isomerism about the double bond of an olefin occurs only if it is in conjugation with an aromatic ring (2). Products in the Crude Butadiene C4 Category do not contain component molecules that will undergo direct photolysis. Therefore, this fate process will not contribute to a measurable degradative removal of chemical components in this category from the environment. **References** 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. Virginia, USA. 2. Harris, J. C. 1982. "Rate of Aqueous Photolysis," Chapter 8 in: W. J. Lyman, W. F. Reehl, and D. H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, USA. 3. Zepp, R. G. and D. M. Cline. 1977. Rates of Direct Photolysis in the Aqueous Environment, Environ. Sci. Technol., 11:359-366.	
Indirect Photolysis:** • **Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life**	Not applicable	
Degradation Products:** • **Note: Identification, concentration**	Unknown	

Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Not applicable
Reliability: (FT - RL)	Not applicable
Reference: (FT - RE)	American Chemistry Council, Olefins Panel. 2002. Hydrolysis: Crude Butadiene C4 Category. Rosslyn, VA, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "photodegradation". Selecting this option refers the reader to information in the "freetext" field for "test substance".

** In IUCLID, provide addtional discussion if needed in the results freetext

FT - Freetext

IUCLID fields include:

- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Photodegradation (Indirect)

Test Substance*:	Other TS
Method/Guideline:	Calculated values using AOPWIN version 1.89, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Type (air, soil, water, other):	Not applicable
Light Source:	Sunlight
Light Spectrum: • **Wave length value (upper/lower)**	Natural sunlight
Relative Intensity:	1
Test Substance Spectrum:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol**	Indirect photodegradation, or atmospheric oxidation potential, is based on the structure-activity relationship methods developed by R. Atkinson. Temperature: 25°C Sensitizer: OH radical Concentration of Sensitizer: $1.5 E^{6}$ OH radicals/cm^3
Direct Photolysis:** **Results: half-life, % degradation, quantum yield**	Not applicable
Indirect Photolysis:** • **Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life**	In the environment, organic chemicals emitted into the troposphere are degraded by several important transformation processes. The dominant transformation process for most compounds is the daylight reaction with hydroxyl (OH-) radicals (1,2). The rate at which an organic compound reacts with OH- radicals is a direct measure of its atmospheric persistence (3). AOPWIN estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The rate constants estimated by the program are then used to calculate atmospheric half-lives for organic compounds based upon

average atmospheric concentrations of hydroxyl radicals.

Since the reactions only take place in the presence of sunlight, the atmospheric half-lives are normalized for a 12-hour day.

Chemical	Calculated* half-life (hrs)	OH- Rate Constant (cm^3/molecule-sec)
Isobutane	52.6	$2.4 E^{-12}$
n-butane	48.8	$2.6 E^{-12}$
isobutylene	2.5	$51.7 E^{-12}$
cis-butene-2	2.3	$56.7 E^{-12}$
trans-butene-2	2.0	$64.3 E^{-12}$
butene-1	4.7	$27.4 E^{-12}$
1,3-butadiene	1.9	$66.6 E^{-12}$

* Atmospheric half-life values are based on a 12-hr day.

Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4.

The seven chemicals selected to represent the atmospheric half-life range of this category are C4 hydrocarbons that are common across the 10 CAS numbers listed under Test Substance. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (4).

References:

1. Atkinson, R. 1988. Estimation of gas-phase hydroxyl radical rate constants for organic chemicals. *Environ. Toxicol. Chem*. **7**:435-442.
2. Atkinson, R. 1989. Kinetics and mechanisms of the gas-phase reactions of the hydroxyl radical with organic compounds. J. Phys. Chem. Ref. Data Monograph No. 1, Amer. Inst. Physics & Amer. Chem. Soc., NY.
3. Meylan, W.M. and P.H. Howard. 1993. Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. *Chemosphere* **12**:2293-2299.
4. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4

	Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Degradation Products:** • **Note: Identification, concentration**	Unknown
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Atmospheric oxidation vial hydroxyl radical can be a significant route of degradation for products in this category. Based on calculated values, products in this category can have an atmospheric half-life range of 1.9 to 52.6 hours as a result of indirect photolysis by hydroxyl radical attack.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include values calculated using the AOPWIN program and represent a potential atmospheric half-life range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. AOPWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "photodegradation". Selecting this option refers the reader to information in the "freetext" field for "test substance".
** In IUCLID, provide additional discussion if needed in the results freetext
FT - Freetext
IUCLID fields include:
RL - Reliability
TC - Test Conditions

RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Hydrolysis (Stability in Water)

Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
Type (test type): **GLP (Y/N):**	Not applicable Not applicable
Year (study performed):	Not applicable
Analytical Monitoring:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration preparation, vessel type, volume, replication, deviations from guideline or protocol**	Not applicable
Results: (FT - RS) **Units/Value:** • **Note: Analytical method, observations, half-lives by pH, degradation products**	Not applicable
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	**Summary** In the environment, hydrolysis will not contribute to the

degradation of chemicals in the Crude Butadiene C4 Category (C4 refers to a chemical with 4 carbons). This category includes two process streams:

- **C4 Crude Butadiene**
- **Butadiene Unit Heavy Ends**

Ten CAS numbers (see Test Substance) identify products derived from these process streams. As discussed below, the chemicals in these streams are composed of carbon and hydrogen and are not amenable to hydrolysis because of their molecular structure and the chemical reaction required for this type of transformation to occur.

The Crude Butadiene C4 Category

A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. Process streams containing 10 to 92% butadiene are referred to as "crude butadiene." The CAS numbers or streams in this category consist of complex mixtures of hydrocarbons.

Most commercial products in this category have a carbon number distribution predominantly between C3 and C5. All of these streams contain significant levels of 1,3-butadiene and olefins, which is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Crude Butadiene C4.

The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process).

Crude butadiene streams arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the two process streams in this category are:

- **C4 Crude Butadiene** is produced by the distillation of a condensed portion of cracked gas in an ethylene process. C4 Crude Butadiene typically contains 40% to about 60% 1,3-butadiene, but could contain between 10% and 82% butadiene. Other chemicals in this mixed stream are

predominately chemicals containing 4 carbons.

- **Butadiene Unit Heavy Ends** is produced by extractive distillation of cracked gas. The 1,3-butadiene content of this mixed stream ranges from 13% to 92%. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. Only three companies report isolating this stream which is more typically an un-isolated intermediate.

Hydrolysis of Hydrocarbons as a Function of Molecular Structure

Hydrolysis of an organic molecule occurs when a molecule (R-X) reacts with water (H_2O) to form a new carbon-oxygen bond after the carbon-X bond is cleaved (2,3). Mechanistically, this reaction is referred to as a nucleophilic substitution reaction, where X is the leaving group being replaced by the incoming nucleophilic oxygen from the water molecule. The leaving group, X, must be a molecule other than carbon because for hydrolysis to occur, the R-X bond cannot be a carbon-carbon bond.

The carbon atom lacks sufficient electronegativity to be a good leaving group and carbon-carbon bonds are too stable (high bond energy) to be cleaved by nucleophilic substitution. Thus, hydrocarbons, including alkenes, are not subject to hydrolysis (3) and this fate process will not contribute to the degradative loss of chemical components in this category from the environment.

Under strongly acidic conditions the carbon-carbon double bond found in alkenes, such as those in the Crude Butadiene C4 Category, will react with water by an addition reaction mechanism (2). The reaction product is an alcohol. This reaction is not considered to be hydrolysis because the carbon-carbon linkage is not cleaved and because the reaction is freely reversible (3).

Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (4). The chemicals in this category are primarily olefins that contain at least one double bond (alkenes). The remaining chemicals are saturated hydrocarbons (alkanes). These two groups of chemicals contain only carbon and hydrogen. As such, their molecular structure is not subject to the hydrolytic mechanism discussed above. Therefore, chemicals in the Crude Butadiene C4 Category have a very low potential to hydrolyze, and this degradative process will not contribute to their removal in the environment.

References

1. Olefins Panel, HPV Implementation Task Group. 2001. High

	Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA. 2. Gould, E.S. (1959), Mechanism and Structure in Organic Chemistry, Holt, Reinhart and Winston, New York, NY, USA. 3. Harris, J.C. (1982), "Rate of Hydrolysis," Chapter 7 in: W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, NY, USA. 4. Neely, W. B. 1985. Hydrolysis. In: W. B. Neely and G. E. Blau, eds. Environmental Exposure from Chemicals. Vol I., pp. 157-173. CRC Press, Boca Raton, FL, USA.
Reliability: (FT - RL)	Not applicable
Reference: (FT - RE)	American Chemistry Council, Olefins Panel. 2002. Hydrolysis: Crude Butadiene C4 Category. Rosslyn, VA, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "hydrolysis". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Transport / Distribution (Fugacity)

Test Substance*:	Other TS
Method/Guideline:	Calculated according to Mackay Level I, EQC Model version 1.01
Year (guide line):	1997
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. Physical properties input into the model are those calculated by the EPIWIN Estimation v 3.04 program (1) or supplied by the databases of experimental values contained with EPIWIN. Output data from the equilibrium model provides basic information on the potential distribution of chemicals between selected environmental compartments (i.e. air, water, soil, sediment, suspended sediment, biota). 1. EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of partitioning data for compone nt chemicals is an estimate of the partitioning behavior for category products. Calculated* Measured** Percent Distribution Percent Distribution Chemical Air Water Air Water Isobutane 99.99 0.01 99.99 0.01 n-butane 99.98 0.02 99.99 0.01 isobutylene 99.98 0.02 99.99 0.01 cis-butene-2 99.97 0.03 99.98 0.02 trans-butene-2 99.97 0.03 99.98 0.02

	butene-1 99.98 0.02 99.99 0.01 1,3-butadiene 99.97 0.03 99.97 0.03 * Distribution values determined using input data calculated by the EPIWIN program **Distribution values determined using input data supplied by the EPIWIN program experimental databases (EXPKOW.DB, EXP_MBVP.DB, and EXP_MBVP.DB) which contain more than 11,000 organic compounds with reliably measured values. Distribution of each chemical to each remaining compartment (soil, sediment, suspended sediment, biota) was calculated as less than 0.01%. Mobility in the environment is expected to be high due to the relatively high water solubility and high vapor pressure of these chemicals. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the transport / distribution range of this category are C4 hydrocarbons that are common across the 10 CAS numbers (see Test Substance) and can represent a significant proportion of a product. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-

	Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Products in the Crude Butadiene C4 Category are expected to distribute to air with a small percentage partitioning to water.
Reliability: (FT - RL)	(2) Reliable with restrictions The input data used to run the EQC Level I model include estimated values calculated by the EPIWIN program based on chemical structure, and experimental values supplied by the EPIWIN program databases. The partitioning data represent a potential distribution range for products with the 10 CAS numbers listed under Test Substance. Computer modeling is an accepted method of assessing environmental distribution of chemicals.
Reference: (FT - RE)	Mackay, D.A. DiGuardo, S. Paterson, and C. Cowan. EQC Model Version 1.01. 1997. Available from the Environmental Modeling Centre, Trent University, Canada.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "transport / distribution". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Biodegradation

Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
Type (test type): **GLP:**	Not applicable Not applicable
Year (study performed):	Not applicable
Inoculum:	Not applicable
Exposure Period:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Not applicable
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Not applicable
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	**SUMMARY** In the environment, biodegradation will not contribute significantly to the loss of chemicals in products from the

Crude Butadiene C4 Category (C4 refers to a chemical with 4 carbons). This category includes two process streams:

- **C4 Crude Butadiene**
- **Butadiene Unit Heavy Ends**

Ten CAS numbers (see Test Substance) identify products derived from these process streams. The products contain various chemicals composed of carbon and hydrogen. As discussed below, products in this category are gaseous. If they are released to the environment, their chemical components will partition primarily to the air where they can degrade rapidly by physicochemical reactions. It is far less likely that products from this category will partition to environmental compartments where they could be degraded by bacteria.

The Crude Butadiene C4 Category

A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. Process streams containing 10 to 92% butadiene are referred to as "crude butadiene." The CAS numbers or streams in this category consist of complex mixtures of hydrocarbons.

Most commercial products in this category have a carbon number distribution predominantly between C3 and C5. All of these streams contain significant levels of 1,3-butadiene and olefins, which is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Crude Butadiene C4.

The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process).

Crude butadiene streams arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the three process streams in this category are:

- **C4 Crude Butadiene** is produced by the distillation of a condensed portion of cracked gas in an ethylene process.

C4 Crude Butadiene typically contains 40% to about 60% 1,3-butadiene, but could contain between 10% and 82% butadiene. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons.

- **Butadiene Unit Heavy Ends** is produced by extractive distillation of cracked gas. The 1,3-butadiene content of this mixed stream ranges from 13% to 92%. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. Only three companies report isolating this stream which is more typically an un-isolated intermediate.

Biodegradation of Hydrocarbons

Biodegradation is the use of a chemical by microorganisms as a source of energy and carbon. The parent chemical is broken down to simpler, smaller chemicals, which can be converted to inorganic forms such as carbon dioxide, nitrate, sulfate, and water.

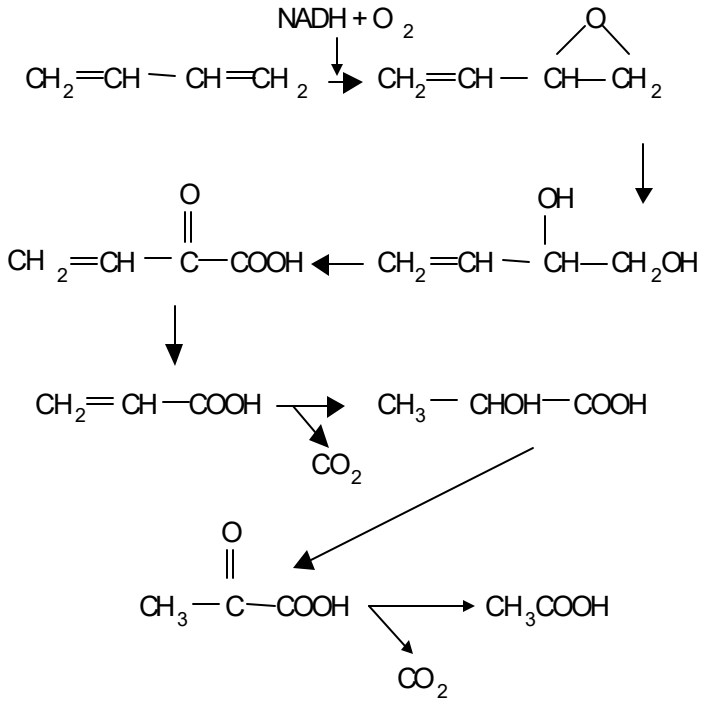
Products in the Crude Butadiene C4 Category are gaseous hydrocarbons, composed predominantly of chemicals with carbon numbers smaller than C5. However, the *Full-Range Butadiene Concentrates* process stream from this category, can contain hydrocarbons greater than C4. These chemicals when isolated individually are not gaseous, but relatively volatile liquids under most environmental conditions.

Several hydrocarbons as well as products that are mixtures of hydrocarbons with carbon numbers greater than C4 have been shown to biodegrade. If released to the environment, biodegradation of these chemicals will occur primarily in aquatic and terrestrial habitats. There is sufficient biodegradation data on hydrocarbons in this category that are greater than C4 to show that these chemicals have a potential to biodegrade to a great extent and not persist in the environment (see the *C5 Noncyclics, Low Benzene Naphtha, and High Benzene Naphtha* HPV Chemical Program test plans from the Olefins Panel of the American Chemistry Council, for specific data and a more detailed discussion of the biodegradability of selected hydrocarbons greater than C4.) The larger proportion of chemicals from this category are gaseous. Consequently, their availability to microbial degraders will be significantly limited.

Component chemicals from all three process streams in this category are simple hydrocarbons, the majority of which will partition primarily to the air where physical processes will contribute to their degradation [see the atmospheric oxidation potential (AOP) data (as mediated by hydroxyl radical

attack) for specific degradation rates of selected chemicals from this category; AOP data were developed for this category under the HPV Chemical Program]. All chemicals from this category that partition to the air are calculated to degrade rapidly due to physical processes and not persist. Because of the partitioning behavior of chemicals in this category, biodegradative processes will be less likely to contribute to their loss from the environment.

Products from the Crude Butadiene C4 Category do not lend themselves to being evaluated for biodegradability using standard experimental techniques because of their physical state. However, there is microbial metabolism information for one of the major chemicals, 1,3-butadiene, in this category that demonstrates that it can be biodegraded. Experimental studies to determine a catabolic pathway for 1,3-butadiene as mediated by a *Nocardia* sp. (3) resulted in the following proposed series of reactions:



The intermediary metabolic steps depicted above result in the production of acetic acid, CH3COOH, which can be further metabolized. In addition, 1,3-butadiene has been estimated to have an aerobic aquatic biodegradation half-life ranging from 1 to 4 weeks (2).

The potential biodegradability of some of the higher molecular weight components including benzene, toluene, xylene, ethylbenzene, and naphthalene has been summarized and metabolic pathways leading to their biodegradation have

	been described (4). These compounds have been shown to biodegrade to high extents such that if they were to partition to either a terrestrial or aqueous environment, they would be subject to biodegradative processes that would result in their removal from the environment. In summary, because the C4 and lighter chemical components of this category will partition to the air, physical degradative processes will dominate their fate. Data show that these chemicals are subject to rapid physical degradation. Chemical components of this category that are greater than C4 also have a potential to partition to the air to a great extent, where they will also degrade rapidly in a similar manner. However, they also have a potential to partition to aquatic and terrestrial environments where they are subject to biological processes that can result in their rapid biodegradation. Overall, products from this category and their component chemicals are expected to degrade rapidly in the environment and not persist. **References** 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. Virginia, USA. 2. Howard, P.H., R.S. Boethling, W.F. Jarvis, W.M. Meylan, and E.M. Michalenko. 1991. Handbook of Environmental Degradation Rates. H.T. Printup Ed. Lewis Publishers, Chelsea, MI, USA. 3. Watkinson, R.J. and H.J. Somerville. 1976. The Microbial Utilization of Butadiene. Shell Research Limited, Sittingbourne Research Centre, Kent, UK. 4. van Agteren, M.H., S. Keuning, and D.B. Janssen. 1998. Handbook on Biodegradation and Biological Treatment of Hazardous Organic Compounds. Kluwer Academic Publishers. Boston, CT, USA.
Reliability: (FT - RL)	Not applicable
Reference: (FT - RE)	American Chemistry Council, Olefins Panel. 2002. Hydrolysis: Crude Butadiene C4 Category. Rosslyn, VA, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "biodegradation". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

HUMAN HEALTH ROBUST SUMMARIES

Acute Toxicity

Test Substance	
Remarks	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	OECD 402.
Type (test type)	Acute inhalation.
GLP	Yes.
Year	1982.
Species/Strain	Rat/Fischer 344.
Sex	Males and females.
No. of animals per sex per dose	5/sex.
Vehicle	Not applicable.
Route of administration	Inhalation (gas).
Test Conditions	A group of ten rats (age: 12 weeks, weight: 143-234 grams) were exposed to 5,300 mg/m3 (2,331 ppm) of the test substance in air for four hours. Analytical chamber concentrations were determined by gas chromatography every 15 minutes during the exposure; a single particle size sample was taken to show the absence of aerosol. Body weights were recorded prior to exposure and 7 and 14 days post-exposure. Individual clinical observations were recorded pre-exposure and daily for 14 days post-exposure. The rats were sacrificed on the fourteenth day and a gross necropsy performed.
Results	
LC50	Rat LC50 (4 hour) = >5,300 mg/m3 (2,331 ppm)
Remarks	Observations noted following exposure were two male rats with respiratory sounds/wheezing or hyperexcitability and one female with minimal porphyrin around the eyes. All rats were normal from Days 2-14. No significant necropsy findings were reported, except one female with an ovary filled with red fluid. Body weight gains appeared normal.
Conclusions	
(study author)	No mortality or significant adverse effects were observed in rats exposed to 5,300 mg/m3 (2,331 ppm) of the test substance.
Data Quality	
Reliability	Reliable without restrictions. Guideline study.
References	Gulf Oil Chemicals Company (1982). Acute LC50 Inhalation Toxicity Test in Rats with Butadiene Feedstock. Unpublished report (Project #82-060).

Other	Robust Summary prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	19-Oct-99

Acute Toxicity

Test Substance	1,3-butadiene CAS# 106-99-0
Method	
Method/guideline followed	Other.
Type (test type)	Acute inhalation.
GLP	Pre-GLP.
Year	1969.
Species/Strain	Rat and mouse (strains not specified).
Sex	Not specified.
No. of animals per sex per dose	Not specified.
Vehicle	Not applicable.
Route of administration	Inhalation (gas).
Test Conditions	Age, number, and sex of test animals not specified. Number of groups and exposure concentrations not specified. Dynamic flow exposure system; no description of exposure chambers or conditions. Rats exposed four hours; mice exposed two hours. No post-exposure observation period - mortality study only. Exposure concentrations "controlled" by gas chromatography.
Results	
LC50 with confidence limits	Rat LC50 (4 hour) = 285 mg/L (219-370 mg/L $p \leq 0.05$) Mouse LC50 (2 hour) = 270 mg/L (251-290 mg/L $p \leq 0.05$)
Remarks	No clinical observations or necropsy findings reported. Objective of study was to determine hydrocarbon concentrations in various tissues at lethal exposure concentrations.
Conclusions	
(study author)	LC50 value reported to be 285 mg/L (129,000 ppm) in rats, 270 mg/L (122,000 ppm) in mice.
Data Quality	
Reliability	Not assignable. Lethality study only; insufficient experimental detail to assess quality.
References	Shugaev, B.B. (1969) Concentrations of Hydrocarbons in Tissues as a Measure of Toxicity. Arch. Environ. Health 18:878-882.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	13-Oct-99

Acute Toxicity

Test Substance	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 67% 1,3-butadiene, 30% butenes, 2% 1,2-butadiene
Method	
Method/guideline followed	Other.
Type (test type)	Irritation screen in rabbits.
GLP	Yes.
Year	1985.
Species/Strain Sex	Rabbit (New Zealand White). 1 male, 1 female.
Vehicle	Not applicable.
Route of administration	Eye and skin.
Remarks For Test Conditions	Two young adult rabbits were evaluated for eye and skin irritation. The test substance was dispensed immediately prior to dosing into a flask packed in dry ice. On the first treatment day, 0.1mL of the test substance was instilled into one eye of each rabbit. Irritation was scored at 24, 48, and 72 hours. The untreated eye served as the control. Twenty-four hours after treatment of the eye, 0.1mL of the test substance was applied to the skin of the rabbits and occluded with a rubber dam. The test sites were evaluated 1, 3, and 7 days after dosing.
Results	
Remarks	The eye irritation scores were 0 at all observation intervals. The treated skin sites were virtually free of irritation at all observation intervals.
Conclusions	
(study author)	The test substance is estimated not to be irritating to the eye or skin.
Data Quality	
Reliability	Reliable with restrictions. Screening study.
References	Mobil Environmental and Health Sciences Laboratory (1985). Irritation Screen of Butadiene Concentrate in Albino Rabbits, Unpublished report (Study No. 41652).
Other	Robust Summary prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	24-Oct-99

Genetic Toxicity - *in vitro*

Test Substance	
Test substance	1,3-butadiene CAS# 106-99-0
Method	
Method/guideline followed	No data.
Type	Reverse mutation assay (Ames *Salmonella* test).
System of testing	Bacterial.
GLP	No data.
Year	1990.
Species/Strain	Salmonella typhimurium/TA97, TA98, TA100, TA1535.
Metabolic activation	With and without.
Species and cell type	Rat, mouse, and human liver S9 fraction.
Quantity	0.8 and 4.0 mg protein/plate.
Induced or not induced	Arochlor 1254-induced and uninduced rat, mouse, and human S9.
Concentrations tested	0, 30, 40, 50, and 60% butadiene in air.
Statistical Methods	Not specified.
Remarks for Test Conditions	Concentrations of butadiene gas were metered into specially constructed treatment chambers holding the agar plates overlaid with the bacteria and activation system. Actual gas concentrations were determined by gas chromatography before and after the 48 hour exposure period. Different treatment chambers were used for each activation system and for the non-activated treatment. S9 preparations were made according to the procedure of Ames *et al.* (1975).
Results	1,3-Butadiene (BD) induced revertants only in strain TA1535. Mouse S9 showed slightly higher activity than the uninduced rat or human S9 at 30% 1,3-butadiene in air. At concentrations greater than 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 treatments. Arochlor 1254-induced rat S9 gave similar results as mouse S9 (uninduced). Since the response was weak, the S9 concentration was increased from 0.8 mg/plate to 4.0 mg/plate. Increasing the concentration of Arochlor 1254-induced rat S9 had no effect on the number of revertants; slightly more revertants were observed using 4.0 than 0.8 mg/plate of uninduced rat S9.
Conclusions	
(study author)	*Salmonella typhimurium* reverse gene mutation (Ames) tests of 1,3-butadiene using strains TA1535, TA97, TA98, and TA100 and employing rat, mouse, and human liver S9 metabolic systems were barely 2-fold above background only in strain TA1535 at 30% butadiene in air with induced and uninduced rat S9 and mouse S9 (uninduced). In general, 1,3-butadiene was a weak *in vitro* genotoxin.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study.
Reference	Arce G.T., Vincent D.R., Cunningham M..J, Choy W.N., and Sarrif

	A.M. (1990). *In vitro* and *in vivo* genotoxicity of 1,3-butadiene and metabolites. Environ. Health Perspect. 86:75-8.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	18-Oct-99

Genetic Toxicity - *in vitro*

Test Substance	
Test substance	Butadiene Concentrate, CAS# 68955-28-2. Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	OECD 482.
Type	Unscheduled DNA Synthesis (UDS).
System of testing	Primary hepatocytes derived from Fischer 344 rats.
GLP	Yes.
Year	1984.
Metabolic activation	No.
Concentrations tested	0, 1000, 5000, 10000, and 20000 ppm.
Control groups and treatment	Negative = air only; positive = 2-acetylaminofluorene (0.2ug/mL).
Statistical Methods	Group means and standard deviations for number of viable cells and nuclear grain counts. The test substance was considered positive if the mean nuclear grain count exceeded the negative control by at least 6 grains per nucleus and the negative control did not exceed 5.
Remarks for Test Conditions	Primary hepatocytes were derived from freshly perfused rat liver (1 male, 10 weeks age, 226 grams body weight). Cultures were seeded with approximately 10^5 cells/mL on Day 1. Three cultures per group were exposed to ^{3}H-thymidine and the test substance for 18-20 hours. The culture flasks were placed in sealed dessicator jars for the exposure period, and the test substance added by injection via a 50cc syringe. Cells growing on coverslips were fixed on Day 2. On Day 3 the slides were dipped in autoradiograph emulsion and stored in the dark at 2-8^{o}C. The autoradiographs were developed and stained on Day 21.
Results	A separate range-finding study was conducted to establish levels of cytotoxicity based on relative cell viability. The test substance was toxic to primary hepatocytes at 10000 ppm where 64% relative viability was observed following 18 hour exposure. At 20000 ppm, the relative viability was 57%. In the UDS study, both positive and negative control groups gave expected responses. A weak positive response was observed at 20000 ppm (7.74 nuclear grain counts vs. 1.24 in the air control vs. 107.13 in the positive control). The 1000, 5000, and 10000 ppm groups were also slightly increased (4.29-5.14) from the air control but less than the criteria for a significant response.
Conclusions (study author)	Cytotoxicity was observed at 10000 ppm. Increased unscheduled DNA synthesis was observed at 20000 ppm.
Data Quality	
Reliabilities	Reliable without restrictions. Guideline study.
Reference	Gulf Oil Chemicals Company (1984). Hepatocyte Primary Culture/DNA Repair Test of Butadiene Feedstock, Unpublished report (Project# 2073).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences,

	Inc.
L*ast changed*	18-Oct-99

Genetic Toxicity - *in vitro*

Test Substance	
Test substance	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	Other.
Type	Mammalian cell transformation test.
System of testing	BALB/3T3-A31-1-1 cells.
GLP *Year*	Yes. 1983.
Metabolic activation	No.
Concentrations tested	0, 1000, 5000, 10000, and 20000 ppm.
Control groups and treatment	Negative = air only; positive = 3-methylcholanthrene (1.0 ug/mL).
Statistical Methods	Group means and standard deviations for number of viable cells, cloning efficiency, and transformed foci per culture. The test substance was considered positive if there was a two-fold increase in foci compared to the negative control group.
Remarks for Test Conditions	Each treatment group consisted of 12 flask cultures for cell transformation seeded with 10000 cells and 2 plate cultures for cloning efficiency with 250 cells. The cultures were placed in sealed dessicator jars and exposed to the test substance for two days. The test substance was added to the jars by injection via a 50cc syringe and samples of the exposure atmosphere were analyzed by gas chromatography. The mediums were changed on Day 4 and then weekly. Plate cultures were fixed and stained on Day 8 and flask cultures on Day 29. Foci in transformation cultures were counted and examined microscopically to determine type.
Results	Cloning efficiency was used as a measure of toxicity under culture conditions. Toxicity was observed at 5000 ppm where a relative cloning efficiency of 53.8% was observed. The negative and positive control gave expected responses for transformation. The response for the test substance was not increased from the negative control group at any level tested.
Conclusions	
(study author)	The test substance was negative for cell transformation.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to draft OECD guideline.
Reference	Gulf Oil Chemicals Company (1983). BALB/3T3 Transformation Test Using Butadiene Feedstock, Unpublished report (Project# 2074).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	18-Oct-99

Genetic Toxicity - *in vitro*

Test Substance	
Remarks	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 67% 1,3-butadiene, 30% butenes, 2% 1,2-buta diene.
Method	
Method/guideline followed	No data.
Type	Reverse mutation assay (Ames *Salmonella* test).
System of testing	Bacterial.
GLP Year	Yes. 1985.
Species/Strain	Salmonella typhimurium/ TA98, TA100, TA1535, TA1537, TA1538.
Metabolic activation	With and without.
Species and cell type	Rat liver S9 fraction.
Quantity	0.6 mL.
Induced or not induced	Arochlor 1254-induced.
Concentrations tested	25, 50, 75, or 100 uL.
Statistical Methods	The test substance was considered mutagenic if it produced a dose-related two-fold increase in mean revertant value compared to the negative control.
Remarks for Test Conditions	The test substance was stored in a dry ice/ethanol slurry to prevent loss of volatile components and dosed by microdispenser into sterile septa-capped culture tubes. Sodium phophate buffer or S-9/bacteria mix was injected through the septa into the tubes containing the test substance and pre-incubated for 20 minutes at 37°C. After the pre-incubation period, the contents of the tubes were overlayed on agar and incubated for 48 hours at 37°C. Revertant colonies were counted by automatic colony counter. Positive control chemicals were: 2.0 ug 2-aminoanthracene, 15.0 ug 9-aminoacridine, 20.0 ug 2-nitrofluorene, and 5.0 ug N-methyl-N-nitro-N-nitrosoguanidine, in 50 µl DMSO per plate.
Results	A preliminary toxicity/initial mutagenicity assay was conducted over a range of 10 to 500 µl per plate in two strains (TA100 and TA1537) with and without S-9. Toxicity was exhibited at ≥75uL in TA100, and ≥100uL in TA1537. Some inconsistencies in toxicity with increasing dose level were noted that were attributed to the volatility of the test substance. Based on the toxicity data, the test substance was tested in the pre-incubation mutagenicity assay at volumes of 25, 50, 75, and 100 µl per plate. None of the five strains with or without induced rat liver S-9 exhibited reversion frequencies substantially different from spontaneous controls in this assay.
Conclusions	
(study author)	The test substance was not considered a mutagen with or without metabolic activation in this test system.
Data Quality	

Reliabilities	Reliable without restrictions. Comparable to guideline study.
Reference	Mobil Environmental and Health Sciences Laboratory (1985). An Ames Salmonella/Mammalian Microsome Mutagenesis Assay For Determination of Potential Mutagenicity of Butadiene Concentrate, Unpublished report (Study No. 41653).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	24-Oct-99

Genetic Toxicity - i*n vitro*

Test Substance	
Remarks	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 67% 1,3-butadiene, 30% butenes, 2% 1,2-butadiene.
Method	
Method/guideline followed	Other.
Type	Mouse lymphoma mutagenesis assay.
System of testing	Mammalian cell.
GLP Year	Yes. 1985.
Species/Strain	Mouse lymphoma cells/ L5178Y (TK+/-; subclone 3.7.2C).
Metabolic activation	With and without.
Species and cell type	Rat liver S9 fraction.
Quantity	4.0 mL.
Induced or not induced	Arochlor 1242/1254-induced.
Concentrations tested	Nonactivated assays: 10.0, 12.5, 15.0, 17.5, 20.0, 22.5, 25.0, 27.5, 30.0, 35.0 40.0, or 45.0 uL/mL media. S-9 activated assays: 2.5, 5.0, 7.5, 10.0, 12.5, 15.0, 17.5, 20. 0, 22.5, or 25.0 uL/mL.
Statistical Methods	The test substance was considered mutagenic if it produced a dose-related or toxicity-related two-fold increase in average mutant frequency compared to the negative controls, at concentrations exhibiting accepta ble total growths (10% or greater).
Remarks for Test Conditions	The positive control chemical for the S-9 activated assays was 7, 12-dimethylbenz[a]anthracene (DMBA) at 2.5 and 5.0 ug/mL, and ethylmethane sulfonate (EMS) for the nonactivated assays at 0.5 and 1.0 uL/mL. An initial toxicity assay was performed with and without activation at concentrations ranging from 10 to 100 uL/mL. The dosing regimen for the mutagenesis assay was designed to produce 10-90% lethality. Six mLs of cell suspension (10^6 cells/mL) were exposed for 3 hours to the test or positive control substances. An expression period of 2 days followed with determinations of cell population densities and growth. Cultures selected for mutant analysis and cloning efficiencies were incubated for 10-12 days.
Results	Without activation, mutant frequencies and total number of mutants were significantly increased at the two highest concentrations (20.0 and 22.5 uL/mL). Although total growth was very low (5.1% and 5.5%), these levels were considered mutagenic since there was no reduction in cloning efficiency. There were no significant differences in mutant frequency for the S-9 activated cultures.
Conclusions	
(study author)	The test substance induced a significant increase in mutant frequency of mouse lymphoma cells without metabolic activation, but was evaluated as non-mutagenic in the presence of S-9 activation.
Data Quality	

Reliabilities	Reliable without restrictions. Comparable to guideline study.
Reference	Mobil Environmental and Health Sciences Laboratory (1985). Evaluation of the Mutagenic Potential of Butadiene Concentrate in the Mouse Lyphoma (L5178Y/TK+/-) Mutagenesis Assay, Unpublished report (Study No. 41654).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	24-Oct-99

Genetic Toxicity - *in vivo*

Test Substance	
Remarks	1,3-butadiene CAS# 106-99-0
Method	
Method/guideline followed Type	Other. Mammalian erythrocyte micronucleus assay.
GLP	No data.
Year	1994.
Species	Rat and mouse.
Strain	Rat: Wistar. Mouse: CB6F1
Sex	Rat: Male. Mouse: Female.
Route of administration	Inhalation (gas).
Doses/concentration levels	0, 50, 200, or 500 ppm.
Exposure period	6 hours/day for 5 days.
Statistical methods	Student's two-tailed t-test for differences between groups.
Remarks for Test Conditions.	Twenty female CB6F1 mice (approximately 25g, 8-10 weeks old) and ten male Wistar rats (300-350g, 10 weeks old) per group were exposed for 5 days, 6 h/day 0, 50, 200, or 500 ppm of 1,3-butadiene (BD) by inhalation. An additional high concentration group of mice was exposed to 1300 ppm. Exposure concentrations were monitored by infrared spectroscopy (rats) and gas chromatography (mice). The animals were sacrificed 1 day after the last exposure and smears of blood and bone marrow erythrocytes were prepared and stained.
Results	In the rats, no effects on micronuclei frequencies were observed either in the peripheral blood or bone marrow at all exposure levels. A slight toxic effect in rat bone marrow cells (decreased polychromatic/normochromatic ratio) was observed at the 500 ppm level. In the mice, a clear dose-dependent increase in micronuclei frequency was observed in both blood and bone marrow cells at all exposure levels tested.
Conclusions	
(study author)	1,3-butadiene was active in inducing micronuclei in peripheral blood and bone marrow erythrocytes in mice at levels $\geq$50 ppm, but not in rats. The genotoxic effects observed in this study parallel the species differences observed in cancer studies.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study.
References	Autio, K., Renzi, L., Catalan, J., Albrecht, O.E., and Sorsa, M. (1994). Induction of Micronuclei in Peripheral Blood and Bone Marrow Erythrocytes of Rats and Mice Exposed to 1,3-Butadiene by Inhalation. Mut. Res. 309:315-320.
	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	25-Oct-99

Genetic Toxicity - i*n vivo*

Test Substance	
Remarks	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	OECD 474
Type	Mammalian erythrocyte micronucleus test
GLP	Yes
Year	1984
Species	Mouse
Strain	Crl:CD-1 BR Swiss
Sex	Male and female
Route of administration	Inhalation (gas)
Doses/concentration levels	10,780; 20,671; 35,430 ppm
Exposure period	2 hours/day for 2 consecutive days
No. of animals per dose	10/sex/group
Control groups and treatment	10/sex negative (air) control; 5/sex positive control (cyclophosphamide, 75 mg/kg intraperitoneal injection)
Statistical methods	Group mean body weights, total polychromatic erythrocytes (PCEs), normochromatic erythrocytes (NORMs), PCEs with micronuclei, and NORMs with micronuclei were compared by t-test ($p<0.05$ = positive).
Remarks for Test Conditions.	Mice were 11 weeks old and 25-42 grams weight at study initiation. Test and control substances were administered on Days 1 and 2. Exposure concentrations determined by gas chromatography. Animals were observed daily and body weights were recorded on Days 1, 3, and 4. Five mice/sex/group were sacrificed on Days 3 and 4 and bone marrow smears prepared; positive controls (5/sex) were sacrificed on Day 3 only.
Results	No mice died during the study; the only clinical observations were an apparent unconsciousness during exposure. There were no significant body weight differences. The negative and positive control groups produced negative and positive resulats, respectively. Mice in the exposed groups showed increased micronuclei formation at all levels in both sexes. Females were statistically increased from control at all levels on Day 3 and at 20,671 ppm and 35,430 ppm on Day 4; males were significantly increased only at 35,430 ppm on both days. There was no significant change in the PCE/NORM ratio in any group.
Conclusions	
(study author)	The test material produced an increased frequency of micronucleated erythrocytes in the bone marrow of mice at all levels tested.
Data Quality	
Reliabilities	Reliable without restrictions. Guideline study.
References	Gulf Oil Chemicals Company (1984). Micronucleus Test in Mouse Bone Marrow: Butadiene Feedstock Administered by

	Inhalation For 2 Hours/Day For 2 Days, Unpublished report (Project #2014).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	13-Oct-99

Repeated Dose Toxicity

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Rubber grade, containing 0.02% t-butyl catechol; purity ≥98.94%.
Method	
Method/guideline followed	Other
Test type	14-week inhalation study
GLP	Yes
Year	1977
Species	Mouse
Strain	B6C3F1
Route of administration	Inhalation (gas)
Duration of test	14 weeks
Doses/concentration levels	0, 625, 1250, 2500, 5000, or 8000 ppm
Sex Exposure period	10 male, 10 female per group 6 hours/day
Frequency of treatment	5 days/week, total of 63 or 64 exposures
Control group and treatment	10 male, 10 female, air-only exposed
Post exposure observation period	Not applicable
Statistical methods	Group means and standard deviations calculated for body weights.
Test Conditions	Groups of 10 mice/sex /group (4-5 weeks age at study initiation) were exposed to various levels of 1,3-butadiene for 6 hrs/day, 5 days/week for 14 weeks (64 exposures). Because four male mice in the high exposure group died by day 4, another 2 groups of 10 male mice each were restarted (control and 8000 ppm). Mice were observed once daily for morbidity and mortality; moribund animals were sacrificed. Body weights were recorded weekly. At the end of the 95 or 93-day (restart) studies, surviving mice were sacrificed. Necropsies were performed and tissues preserved. Histopathologic examinations were performed on all controls, high exposure (8000 ppm), and early deaths.
Results	
NOAEL (NOEL)	1250 ppm.
LOAEL (LOEL)	2500 ppm, based on reduced body weight gains.
Remarks	Six of ten males and 1/10 females exposed at 8000 ppm, 6/10 males and 1/10 females at 5000 ppm, and 1/10 males at 2500 or 1250 ppm died prior to study termination or were sacrificed in a moribund condition. Body weight gains were decreased in males at 2500, 5000, and 8000 ppm, and at 5000 and 8000 ppm in the females. No exposure-related histopathologic effects were observed in the high (8000 ppm) group.
Conclusions	Based on the results of this study, exposure levels of 625 and 1250 ppm were selected for a 2-year carcinogenicity study in

	mice based on reduced body weight gains and mortality in higher exposure groups.
Data Quality	
Reliabilities	Reliable with restrictions. Acceptable, well-documented study report but deficient by current guidelines. No organ weights, hematology or clinical chemistry evaluations were performed.
References	National Toxicology Program, Toxicology and Carcinogenesis Studies of 1,3-Butadiene (CAS No. 106-99-0) in B6C3F1 Mice (Inhalation Studies), NTP Technical Report Series No. 288, NIH Publication 84-2544 (1984).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	8-Dec-99

Repeated Dose Toxicity

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity >99.2%, containing 120 ppm t-butyl catechol.
Method	
Method/guideline followed	Other.
Test type	13-week inhalation study.
GLP	No data.
Year	1977.
Species	Rat.
Strain	CD (Sprague-Dawley).
Route of administration	Inhalation (gas).
Duration of test	14 weeks.
Doses/concentration levels	0, 1000, 2000, 4000, or 8000 ppm.
Sex	40 male, 40 female per group.
Exposure period	6 hours/day.
Frequency of treatment	5 days/week for 13 weeks.
Control group and treatment	40 male, 40 female, exposed to filtered air only.
Post exposure observation period	Not applicable.
Statistical methods	Analysis of variance for body weights, food consumption, urinalysis, hematology, clinical chemistry, organ weights.
Test Conditions	Groups of 40 rats/sex /group (approx. 5 weeks age at study initiation) were exposed to various levels of 1,3-butadiene for 6 hrs/day, 5 days/week for 13 weeks. All animals were observed daily; individual body weights and food consumption were recorded weekly. Interim sacrifices of 10 rats/sex/group were performed after 2 and 6 weeks of exposure. Three urine samples were obtained from each animal during the 1-2 weeks prior to sacrifice. Blood samples were collected from all rats prior to the 2, 6, and 13 week sacrifices. Brain cholinesterase activity was measured using half the brain of 5 rats/sex/group at the 2 and 6-week sacrifices and all rats at the terminal sacrifice. Organ weights were recorded for the adrenals, brain, gonads, heart, kidneys, liver, lung, pituitary, spleen, and thyroid. Necropsies were performed and tissues preserved. Histopathologic examinations were performed on all control and high exposure (8000 ppm) tissues.
Results	
NOAEL (NOEL)	8000 ppm.
LOAEL (LOEL)	>8000 ppm.
Remarks	Increased salivation was observed in the females after 8 weeks exposure and decreased grooming (stained fur) in the males after 10 weeks. No other exposure-related conditions were observed. Male rats showed slight (non-statistically significant) reductions in body weight gains compared to the controls; female body weights at 1000 and 4000 ppm were statistically higher than the controls.

	Neuromuscular function tests using a modified rotating cone gave some random group differences, but were not considered exposure-related. There were no toxicologically significant differences in hematology, blood chemistry, brain cholinesterase measurements, or urine analysis. Organ weight and organ to brain weight ratios showed some scattered statistically significant differences among the groups but did not indicate any treatment-related effects. Microscopic examination of the tissues of the exposed rats showed a similar incidence and severity of histopathologic findings to the control group.
Conclusions	
(study author)	Rats exposed to butadiene gas at concentrations up to 8000 ppm showed no significant effects related to exposure.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study.
References	Crouch, C.N., Pullinger, D.H., and Gaunt, I.F. (1979) Inhalation Toxicity Studies With 1,3-butadiene - 2. 3 Month Toxicity Study in Rats. Am. Ind. Hyg. Assoc. J. 40:796-802.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	18-Oct-99

Repeated Dose Toxicity

Test Substance	
Remarks	Butadiene feedstock, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	Other.
Test type	9-day inhalation study.
GLP	Yes
Year	1982
Species	Rat
Strain	Fischer 344
Route of administration	Inhalation (gas)
Duration of test	12 days (9 exposures)
Doses/concentration levels	0, 2500, and 25100 mg/m3 (0, 1110, and 11140 ppm)
Sex	5 male, 5 female per group.
Exposure period	6 hours/day.
Frequency of treatment	9 exposure days
Control group and treatment	5 male, 5 female, exposed to air only.
Post exposure observation period	Not applicable.
Statistical methods	Bartlett's test and analysis of variance for body and organ weights. If the Bartlett's test indicated homogeneity, Dunnett's test was also performed; if non-homogeneous, a modified t-test was done.
Remarks for Test Conditions	Three groups of 5 rats/sex /group (8 weeks age and 120-198 grams at study initiation) were exposed to 0, 2500, or 25100 mg/m3 of the test substance for 6 hrs/day for a total of 9 exposures. The exposure regimen was 5 days of exposure , 2 days off, 4 days of exposure, then one day for the terminal sacrifice (12 days). Analytical chamber concentrations were determined by gas chromatography, 5 to 16 times per day in the low and high exposure chambers or approximately every 1.5 hours for the control chamber. A particle size sample was performed once daily for each exposure chamber to confirm the absence of aerosol. Individual animal observations were performed twice daily on exposure days and once daily on non-exposure days. Body weights were recorded prior to the first exposure and on Days 1, 7, and 12. Blood samples were obtained from all rats prior to sacrifice on Day 12. A gross necropsy was performed and organ weights recorded for the brain, heart, kidneys, liver, lung, and spleen. These organs plus the testes and ovaries were preserved and examined microscopically.
Results	
NOAEL (NOEL)	11140 ppm
LOAEL (LOEL)	>11140 ppm
Remarks	Most rats in both exposure groups appeared normal throughout

Conclusions	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 statistically significant 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 and tissues examined.
(study author)	The 9-day repeated inhalation exposure of up to 11140 ppm (25100 mg/m3) resulted in no significant adverse effects in rats.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study (OECD 412).
References	Gulf Oil Chemicals Company (1983). Nine-day Repeated Dose Inhalation Study in Rats Using Butadiene Feedstock, Unpublished report (Project #82-090). (1983). Gulf Life Sciences Center, Pittsburgh PA
Other	Robust summary prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	19-Oct-99

Developmental Toxicity/Teratogenicity

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity 99.88%
Method	
Method/guideline followed	OECD 414.
Test type	Developmental toxicity (teratogenicity) study.
GLP	Yes.
Year	1987.
Species	Mouse.
Strain	CD-1 (Swiss).
Route of administration	Inhalation (gas).
Concentration levels	0, 40, 200, or 1000 ppm.
Sex	18-22 pregnant females per group.
Exposure period	Days 6-15 of gestation.
Frequency of treatment	6 hours/day.
Control group and treatment	Air-exposed only.
Duration of test	Females sacrificed on gestation day 18.
Statistical methods	Analysis of variance for body weights, number of resorptions, implants, live, dead or affected fetuses per litter. Significant differences among the groups were also analyzed by Duncan's multiple range test or arcsin transformation of the response proportion. Binary-response variables were between groups were compared using chi-square or Fisher's exact test.
Remarks for Test Conditions.	Female mice were mated to unexposed males and exposed from days 6-15 of gestation to 0, 40, 200, or 1000 ppm of the test substance. Analytical chamber concentrations were measured by on-line gas chromatography. Body weights were recorded on gestation days 0, 6, 11, 16, and 18. Maternal animals were observed daily for mortality, morbidity, and signs of toxicity and examined for gross tissue abnormalities at necropsy (day 18). The uterus and placenta was removed and weighed; the number of implantation sites, resorptions, live and dead fetuses were recorded. Live fetuses were weighed and subjected to external, visceral, and skeletal examinations. Approximately 50% of the fetal heads were sectioned and examined.
Results	
NOAEL maternal toxicity	40 ppm.
NOAEL developmental	40 ppm.
toxicity	There were decreases in maternal body weight gains in the 200 and 1000 ppm groups. Fetal weights were significantly reduced in both males and females at 200 and 1000 ppm; placenta weights were significantly reduced for corresponding male fetuses at 200 ppm and for 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 sternebrae) at 200 and 1000 ppm.
Conclusions	

(study author)	Developmental toxicity was observed in mice in the presence of maternal toxicity at 200 and 1000 ppm. A slight statistically significant decrease in male fetal weight (95% of control) was also observed, but the biological significance of this finding has been questioned.
Data Quality	
Reliabilities	Reliable without restrictions. Guideline study.
References	Morrissey, R.E., Schwetz, B.A., Hackett, P.L., Sikov, M.R., Hardin, B.D., McClanahan, B.J., Decker, J.R., and Mast, T.J. (1990). Overview of Reproductive and Developmental Toxicity Studies of 1,3-Butadiene in Rodents. Environ. Health Perspect. 86:79-84.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
La*st changed*	20-Oct-99

Developmental Toxicity/Teratogenicity

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity 99.88%
Method	
Method/guideline followed	OECD 414.
Test type	Developmental toxicity (teratogenicity) study.
GLP	Yes.
Year	1987.
Species	Rat.
Strain	CD (Sprague-Dawley).
Route of administration	Inhalation (gas).
Concentration levels	0, 40, 200, or 1000 ppm.
Sex	24-28 pregnant females per group.
Exposure period	Days 6-15 of gestation.
Frequency of treatment	6 hours/day.
Control group and treatment	Air-exposed only.
Duration of test	Females sacrificed on gestation day 20.
Statistical methods	Analysis of variance for body weights, number of resorptions, implants, live, dead or affected fetuses per litter. Significant differences among the groups were also analyzed by Duncan's multiple range test or arcsin transformation of the response proportion. Binary-response variables between groups were compared using chi-square or Fisher's exact test.
Remarks for Test Conditions.	Female rats were mated to unexposed males and exposed from days 6-15 of gestation to 0, 40, 200, or 1000 ppm of the test substance. Analytical chamber concentrations were measured by on-line gas chromatography. Body weights were recorded on gestation days 0, 6, 11, 16, and 20. Maternal animals were observed daily for mortality, morbidity, and signs of toxicity and examined for gross tissue abnormalities at necropsy (day 20). The uterus and placenta was removed and weighed; the number of implantation sites, resorptions, live and dead fetuses were recorded. Live fetuses were weighed and subjected to external, visceral, and skeletal examinations. Approximately 50% of the fetal heads were sectioned and examined.
Results	
NOAEL maternal toxicity	200 ppm
NOAEL developmental	1000 ppm
toxicity	The only toxicity 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 significant 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.
Conclusions	

(study author)	There was no evidence of teratagenicity or adverse reproductive effects in any of the exposed groups.
Data Quality	
Reliabilities	Reliable without restrictions. Guideline study.
References	Morrissey, R.E., Schwetz, B.A., Hackett, P.L., Sikov, M.R., Hardin, B.D., McClanahan, B.J., Decker, J.R., and Mast, T.J. (1990). Overview of Reproductive and Developmental Toxicity Studies of 1,3-Butadiene in Rodents. Environ. Health Perspect. 86:79-84.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
La*st changed*	20-Oct-99

Toxicity to Reproduction

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity 99.88%
Method	
Method/guideline followed	Other.
Test type	Sperm-head morphology assay.
GLP	Yes.
Year	1987.
Species	Mouse.
Strain	B6C3F1.
Route of administration	Inhalation (gas).
Concentration levels	0, 200, 1000, and 5000 ppm.
Sex	20 males per group.
Exposure period	6 hours/day.
Frequency of treatment	5 days.
Control group and treatment	Air-exposed only.
Duration of test	Males sacrificed 5 weeks post-exposure.
Statistical methods	Normal and abnormal sperm heads were expressed as percentage of the total number of cells examined. These data were subjected to arcsin transformation and evaluated by analysis of variance. If significant, Duncan's multiple range test was used for intergroup differences. Dose response trends were determined by orthogonal contrast.
Remarks for Test Conditions.	The mice were observed twice daily and body weights recorded weekly. During the fifth week post-exposure the mice were sacrificed and examined for lesions of the reproductive tract and other gross abnormalities. Sperm was obtained from the cauda of the right epididymis. Slides were prepared, stained, and examined microscopically. The morphology of at least 500 sperm heads per mouse was categorized.
Results	
NOAEL	200 ppm The percentage of abnormal sperm heads increased with exposure concentration: 1.61% (0 ppm), 1.95% (200 ppm), 2.79% (1000 ppm), and 3.79% (5000 ppm). Only the values for the 1000 and 5000 ppm groups were significantly different from the control ($p < 0.05$). Only a single timepoint was examined, so the effect on all stages of spermatogenesis could not be determined.
Conclusions	
(Study author)	These results suggest that the test substance affected spermatogenesis in mice at 1000 and 5000 ppm, but the effect of this observation on other reproductive endpoints is not known.
Data Quality	
Reliabilities	Reliable with restrictions. Acceptable, well-documented publication which meets basic scientific principles.
References	Morrissey, R.E., Schwetz, B.A., Hackett, P.L., Sikov, M.R.,

	Hardin, B.D., McClanahan, B.J., Decker, J.R., and Mast, T.J. (1990). Overview of Reproductive and Developmental Toxicity Studies of 1,3-Butadiene in Rodents. Environ. Health Perspect. 86:79-84.
Other	Robust Summaries Prepared by ExxonMobil Biomedical Sciences, Inc.
Las*t changed*	20-Oct-99

Toxicity to Reproduction

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity 99.88%
Method	
Method/guideline followed	Other.
Test type	Rodent dominant lethal test.
GLP	Yes.
Year	1987.
Species	Mouse
Strain	CD-1 (Swiss).
Route of administration	Inhalation (gas).
Concentration levels	0, 200, 1000, and 5000 ppm.
Sex	20 males per group.
Exposure period Frequency of treatment	6 hours/day. 5 days.
Control group and treatment	Air-exposed only.
Duration of test	8 weeks post-exposure.
Statistical methods	The number of implantation sites and intrauterine deaths per litter for each week were analyzed by analysis of variance. When appropriate, proportions of resorptions and dead or live fetuses per implant were subjected to arcsin transformation and evaluated by analysis of variance. If significant, Duncan's multiple range test was used for intergroup differences.
Remarks for Test Conditions.	After five days of exposure, the male mice were mated with unexposed females (two females per week for each male for 8 consecutive weeks). Females were removed from cohabitation after 7 days sacrificed 12 days later and the uterine contents examined. Observations included: the total number, position, and status of implantations; the numbers of early and late resorptions; and numbers of live and dead fetuses.
Results	Slight statistically significant effects were noted in the mated females for three endpoints during the first 2 weeks post-exposure: ratio of dead to total implants, percentage of females with $\geq$2 dead implants, and number of dead implants per pregnancy. However, these observations only occurred in the two lower exposure groups (except for increased number dead implants/pregnancy in the 5000 ppm group during week 1). There were no differences for number of pregnant females, implantations per litter, number of live fetuses, dead implantations per total implantations, or number of resorptions during weeks 1 and 2. There were no differences for any endpoint during weeks 3-8.
Conclusions	
(Study author)	The authors concluded that the results observed during the first two weeks are consistent with an adverse effect on more mature germ cells (spermatozoa and spermatids) however considering the lack of effects in the high exposure group the findings are not clear for a

	dose-dependent response.
Data Quality	
Reliabilities	Reliable with restrictions. Acceptable, well-documented publication which meets basic scientif ic principles.
References	Morrissey, R.E., Schwetz, B.A., Hackett, P.L., Sikov, M.R., Hardin, B.D., McClanahan, B.J., Decker, J.R., and Mast, T.J. (1990). Overview of Reproductive and Developmental Toxicity Studies of 1,3-Butadiene in Rodents. Environ. Health Perspect. 86:79-84.
Other	Robust Summary Prepared by Exxon Biomedical Sciences, Inc.
La*st changed*	20-Oct-99

Genetic Toxicity - *in vivo*

Test Substance	
Remarks	C4 Crude Butadiene (Low 1,3-Butadiene Content) approx. composition: 10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% trans-2-butene, 29% 1-butene, 11% isobutylene, 12% cis-2-butene Primary CAS #: 68476-52-8 Other CAS #s in the stream: 25167-67-3, 64742-83-2, 68187-60-0, 68476-44-8, 68955-28-2, and 68956-54-7.
Method	
Method/guideline followed Type	U.S. EPA OPPTS 870.5395 (1998) and OECD # 474 (1997) guidelines. Mammalian erythrocyte micronucleus assay.
GLP	Yes.
Year	2001.
Species	Mouse.
Strain Sex	B6C3F1 Male and Female
Route of administration	Inhalation (gas).
Doses/concentration levels	0, 0.5, 10.0, or 20.0 mg/L.
Exposure period	4 hours/day for 2 days.
Statistical methods	The raw data on the counts of MN-PCE for each animal were first transformed by adding one (1) to each count and then taking the natural log of the adjusted number. The transformed MN-PCE data and the data on percent PCE were analyzed separately by a two-way analysis of variance (Winer, 1971). The sex-by-dose interaction in the two-way analysis was reviewed and if significant, a one-way analysis was performed for each sex. Pairwise comparisons of treated vs. control groups were done, if the dose effect was significant, by Dunnett's t-test, one-sided (upper) for MNPCE and two-sided for the percent PCE (Winer 1971). Linear dose-related trend tests were performed only if any of the pairwise comparisons yielded significant differences. The alpha level at which all tests were conducted was 0.05.
Remarks for Test Conditions.	Groups of six male B6C3F1 mice (approximately 26g, 9 weeks old) and six female B6C3F1 mice (approximately 21g, 9 weeks old) were exposed whole-body inhalation to target concentrations of 0, 0.5, 10.0, and 20.0 mg/L of the C4 Crude Butadiene, Low 1,3-Butadiene Content. All inhalation exposures occurred under dynamic airflow conditions and chamber concentrations were monitored by analytical methods. Inhalation exposures occurred on two consecutive days, 4 hours per day. A positive control group was dosed by oral gavage with 120 mg/kg of cyclophosphamide approximately 24 hours before sacrifice. Groups of animals (6/sex/dose) were sacrificed at 24 hours after the second treatment for the collection of femoral bone marrow to evaluate the incidence of micronuclei (MN) in polychromatic erythrocytes (2000 PCE/animal) The proportion of PCE among erythrocytes in the bone marrow was estimated by examining 200

	erythrocytes/animal.
Results	Statistically significant increases in the frequencies of MN-PCE in both sexes of all groups treated with the test material were observed as compared to the negative controls. Although statistical analyses indicated a significant dose response, the difference in MN-PCE incidence at the high- (20 mg/L) and low- (0.5 mg/L) dose was minimal. The positive control treatment induced a significant increase in the frequency of MN-PCE. The mean proportion of PCE among the erythrocytes (200/animal) in the bone marrow was not affected following exposure to the test material while the positive control treatment significantly reduced this value.
Conclusions	
(study author)	C4 Crude Butadiene (low 1,3-butadiene content) was positive for the induction of micronuclei in this test system under the experimental conditions used.
Data Quality	
Reliabilities	Reliable without restrictions.
References	Organisation for Economic Co-Operation and Development (OECD) (1997). Guidelines for Testing of Chemicals. #474. Genetic Toxicology: Micronucleus Test, OECD Publication Service, 2 Rue Andre-Pascal, 75775 Paris Cedex 16, France. U.S. EPA (1998). Office of Prevention, Pesticides and Toxic Substances, OPPTS 870.5395. *In Vivo Mammalian Bone Marrow Cytogenetic Tests - Micronucleus assay* Winer, B. J. (1971). *Statistical Principles in Experimental Design* (2nd Edition). McGraw-Hill, New York, New York. Spencer, T.J., Hammond, T.A., Houtman, C.E. and Marty, G.T. (2001). The valuation of C4 crude butadiene (low 1,3-butadiene content) in the mouse bone marrow micronucleus test by an inhalation exposure - multiple exposures followed by a single sampling point. Report of The Dow Chemical Company conducted for the American Chemistry Council, Olefins Panel.
Other	Last updated: Robust summary prepared by contractor to Olefins Panel

Repeated Dose Toxicity

Test Substance	
Remarks	C4 Crude Butadiene (low 1,3-Butadiene Content), approx. composition: 10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% trans-2-butene, 29% 1-butene, 11% isobutylene, 12% cis-2-butene Primary CAS#: 68476-52-8; Other CAS #s used to represent this stream : 25167-67-3, 64742-83-2, 68187-60-0, 68476-44-8, 68955-28-2, and 68956-54-7
Method	
Method/guideline followed	OECD 422
Test type	Combined repeated exposure inhalation toxicity study with the reproduction / developmental screening test
GLP	Yes
Year	2001
Species	Rat
Strain	Crl:CD® (Sprague-Dawley) IGS BR
Route of administration	Inhalation (vapor).
Duration of test	36-37 days
Doses/concentration levels	0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3)
Sex	12 male, 12 female per group.
Exposure period	6 hours/day.
Frequency of treatment	7 days/week
Control group and treatment	12 male, 12 female, air-only exposed.
Post exposure observation period	Not applicable.
Statistical methods	Adult body weights, body weight gains, feed consumption, organ weights, clinical chemistry data and appropriate hematologic data were evaluated by ANOVA. Detailed clinical observation incidence scores for ranked observations and sensory evaluation scores were statistically analyzed by a z-test of proportions. Rectal temperature and grip performance were analyzed by an analysis of covariance with dose as the factor and time as the covariate. Motor activity was analyzed by a repeated-measure design with treatment as a between-subjects factor and the repeated factor of time.
Test Conditions	Groups of 12 male and 12 female CD rats were exposed to vapors of the test material daily by inhalation for approximately six hours/day at exposure levels of 0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3). The main study (repeated-exposure general toxicity and neurotoxicity endpoints) males and females were exposed for 36 and 37 days, respectively. Effects on general toxicity, neurobehavioral activity, clinical chemistry, and hematology were evaluated. In addition, a gross necropsy with extensive histopathologic examination of tissues was conducted. The study also contained reproductive and developmental toxicity satellite groups (summarized separately).

Results	
NOAEL (NOEL)	20 mg/L (20,000 mg/mg^3).
LOAEL (LOEL)	Not applicable.
Remarks	Actual time-weighted averages for total olefins for the 2, 10 and 20 mg/L (2,000; 10,000; or 20,000 mg/m^3) exposure groups were **2.17** $\pm$ 0.461, **9.81** $\pm$ 1.66, **19.1** $\pm$ 2.63 mg/L, respectively, over the 37 exposure days in the study. Owing in part to the nature of the test material, there were technical difficulties in generating vapors from the test material, such that targeted exposure concentrations were not met on one entire day and for brief periods on a few other days. However, the affected instances were limited relative to the total duration of the study and were considered to have no significant impact on study integrity. There were no deaths or treatment-related clinical observations noted. No significant differences in body weights or feed consumption were observed for the males or females at any dose level tested throughout the duration of the study. Sensory evaluation, rectal temperature, and fore/hindlimb grip performance data revealed no treatment-related findings. Treatment did not affect motor activity total counts (treatment-by-time interaction, p = 0.0930). However, the treatment-by-time-by-epoch interaction was significant (p = 0.0098). Examination of the data suggested that this effect could be reasonably attributed to the significant time-by-epoch interaction (p = 0.0001) rather than to a true treatment effect. This was confirmed following calculation of linear contrasts to determine which group(s), if any, were different from the control group. These analyses revealed that none of the three treatment groups were significantly different from control (alpha > 0.02) when the time-by-epoch-by-treatment interaction was considered. There were no treatment-related changes for males and females at any dose level for prothrombin time, hematology values or clinical chemistry measures. Females exposed to 2 mg/L had a statistically identified increase in hematocrit value, and a statistically identified decrease in serum total protein. Given the lack of dose response, effects on related parameters, and similar effects in males, these were considered incidental findings that were toxicologically insignificant. There were no effects of exposure on organ weights, gross pathology or histopathology in any of the treated groups when compared to their respective controls.
Conclusions	Repeated inhalation exposure of C4 Crude Butadiene, Low 1,3-Butadiene to male and female Sprague Dawley rats at levels of 0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3) produced no evidence of any adverse effects on clinical observations, organ weights, gross or histopathology, neurobehavioral activity, clinical chemistry or hematology endpoints. Based on these data, the no-observable-effect level

	(NOEL) for repeated dose toxicity was 20 mg/L, the highest concentration tested.
Data Quality	
Reliabilities	Klimisch value = 1 (Reliable without restrictions).
References	Carney, E.W., Liberacki, A.B., Thomas, J., Houtman, C.E. and Marable, B.R. (2001). C4 Crude butadiene, low 1,3-butadiene content: a combined repeated exposure inhalation toxicity study with the reproduction/developmental screening test in Sprague Dawley rats. Report of The Dow Chemical Company conducted for the American Chemistry Council, Olefins Panel.
Other	
Last changed	6-Aug-01 Robust summary prepared by contract to Olefins Panel

Toxicity to Reproduction

Test Substance	
Remarks	C4 Crude Butadiene (low 1,3-Butadiene Content) approx. composition: 10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% trans-2-butene, 29% 1-butene, 11% isobutylene, 12% cis-2-butene Primary CAS#: 68476-52-8; Other CAS #s used to represent this stream: 25167-67-3, 64742-83-2, 68187-60-0, 68476-44-8, 68955-28-2, and 68956-54-7
Method	
Method/guideline followed	OECD 422
Test type	Combined repeated exposure inhalation toxicity study with the reproduction / developmental screening test
GLP	Yes.
Year	2001
Species	Rat
Strain	Crl:CD® (Sprague-Dawley) IGS BR
Route of administration	Inhalation (vapor).
Duration of test	Two weeks prior to breeding, during breeding (up to two weeks), and continuing through day 19 of gestation. The dams were then allowed to deliver their litters, which were retained until postnatal day 4. The males were exposed for 36-37 days.
Doses/concentration levels	0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3)
Sex	12 male, 12 female per group.
Exposure period	6 hours/day.
Frequency of treatment	7 days/week
Control group and treatment	12 male, 12 female, air-only exposed.
Post exposure observation period	Not applicable.
Statistical methods	Adult body weights and feed consumption, maternal body weight gains, and pup body weights were analyzed by ANOVA. Gestation length, average time to mating (precoital interval) and litter size were analyzed using a nonparametric ANOVA. Pregnancy rates and mating, conception, fertility and gestation indices were analyzed by the Fisher exact probability test. Evaluation of the neonatal sex ratio was performed by the binomial distribution test. Post-implantation loss, pup survival indices, and other incidence data among neonates were analyzed using the litter as the experimental unit by a censored Wilcoxon test.
Test Conditions	Groups of 12 male and 12 female Sprague Dawley rats were exposed to vapors of the test material daily by inhalation for approximately six hours/day at exposure levels of 0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3). The study design included a main study for repeated dose toxicity end points (summarized separately) and reproductive / developmental toxicity satellite groups of 12 females per exposure level. The reproductive and developmental toxicity satellite groups were

	exposed for two weeks prior to breeding, during breeding (up to two weeks), and continuing through day 19 of gestation. Males from the main study were used to breed these females. The dams were allowed to deliver their litters, which were retained until postnatal day 4. Effects on general toxicity, gonadal function, mating behavior, implantation, and general fertility were evaluated in the satellite group adults, followed by a gross necropsy of the satellite group females on lactation day 5. Litter size, pup survival, sex, body weight, and the presence of gross external malformations was assessed in the offspring. The males were exposed for a total of 36 to 37 days, and were then necropsied. In addition to the repeated dose toxicity end points assessed (discussed separately), reproductive assessment of the males included mating, conception and fertility indices, reproductive organ weights and gross/histopathology of the reproductive tract. Testis histopathology included a qualitative assessment of stages of the spermatogenic cycle.
Results	
NOAEL (NOEL)	20 mg/L (20,000 mg/mg^3).
LOAEL (LOEL)	Not applicable.
Remarks	Actual time-weighted averages for total olefins for the 2, 10 and 20 mg/L (2,000; 10,000; or 20,000 mg/m^3) exposure groups were **2.17** $\pm$ 0.461, **9.81** $\pm$ 1.66, **19.1** $\pm$ 2.63 mg/L, respectively, over the 37 exposure days in the study. Owing in part to the nature of the test material, there were technical difficulties in generating vapors from the test material, such that targeted exposure concentrations were not met on one entire day and for brief periods on a few other days. However, the affected instances were limited relative to the total duration of the study and were considered to have no significant impact on study integrity. There were no deaths or treatment-related clinical observations noted. No significant differences in parental body weights, body weight gains or feed consumption were observed at any dose level tested throughout the duration of the study. The only exception to this was a statistically identified increase in feed consumption noted for the 10 mg/L satellite females during the premating period (days 7-14). However, this increase was considered spurious, as feed consumption increases were not noted during subsequent gestation and lactation periods and similar changes in feed consumption were not observed at the highest exposure level of 20 mg/L. There were no treatment-related effects at any dose level on any of the reproductive parameters evaluated in this study. These included measures of reproductive performance (mating, conception and fertility, time to mating, gestation length, litter size), offspring survival (gestation and postnatal survival indices, percent pre- and post-implantation loss), pup body weight and pup sex ratio. The only statistically identified

	change in any of these parameters was an increase in post-implantation loss occurring only at the low-dose. This was considered a spurious finding, given the lack of a dose response. Of the 12 females mated in each group, the number of viable litters produced was 11, 11, 11, and 12 for the 0, 2, 10 and 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3) exposure level groups, respectively. External morphological alterations observed in the pups were limited to a hernia observed in a single pup from the high dose group. Given the low incidence of this finding, it was considered spurious and unrelated to exposure.
Conclusions	Repeated inhalation exposure of C4 Crude Butadiene, Low 1,3-Butadiene to male and female Sprague Dawley rats at levels of 0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3) produced no evidence of adverse effects on any measures of reproductive function. Based on these data, the no-observable-effect level (NOEL) for reproductive toxicity was 20 mg/L, the highest concentration tested.
Data Quality	
Reliabilities	Klimisch value = 1 (Reliable without restrictions).
References	Carney, E.W., Liberacki, A.B., Thomas, J., Houtman, C.E. and Marable, B.R. (2001). C4 Crude butadiene, low 1,3-butadiene content: a combined repeated exposure inhalation toxicity study with the reproduction/developmental screening test in Sprague Dawley rats. Report of The Dow Chemical Company conducted for the American Chemistry Council, Olefins Panel.
Other	
Last changed	6-Aug-01 Robust summary prepared by contractor to Olefins Panel

Developmental Toxicity/Teratogenicity

Test Substance	
Remarks	C4 Crude Butadiene (low 1,3-Butadiene Content), approx. composition: 10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% trans-2-butene, 29% 1-butene, 11% isobutylene, 12% cis-2-butene Primary CAS#: 68476-52-8; Other CAS #s used to represent this stream : 25167-67-3, 64742-83-2, 68187-60-0, 68476-44-8, 68955-28-2, and 68956-54-7
Method	
Method/guideline followed	OECD 422
Test type	Combined repeated exposure inhalation toxicity study with the reproduction / developmental screening test
GLP	Yes.
Year	2001
Species	Rat
Strain	Crl:CD® (Sprague-Dawley) IGS BR
Route of administration	Inhalation (vapor).
Duration of test	Two weeks prior to breeding, during breeding (up to two weeks), and continuing through day 19 of gestation. The dams were then allowed to deliver their litters, which were retained until postnatal day 4.
Doses/concentration levels	0, 2, 10, or 20 mg/L
Sex	12 male, 12 female per group.
Exposure period	6 hours/day.
Frequency of treatment	7 days/week
Control group and treatment	12 male, 12 female, air-only exposed.
Post exposure observation period	Not applicable.
Statistical methods	Adult body weights and feed consumption, maternal body weight gains, and pup body weights were analyzed by ANOVA. Gestation length, average time to mating (precoital interval) and litter size were analyzed using a nonparametric ANOVA. Pregnancy rates and mating, conception, fertility and gestation indices were analyzed by the Fisher exact probability test. Evaluation of the neonatal sex ratio was performed by the binomial distribution test. Post-implantation loss, pup survival indices, and other incidence data among neonates were analyzed using the litter as the experimental unit by a censored Wilcoxon test.
Test Conditions	Groups of 12 male and 12 female Sprague Dawley rats were exposed to vapors of the test material daily by inhalation for approximately six hours/day at exposure levels of 0, 2, 10, or 20 mg/L. The study design included a main study for repeated dose toxicity end points (summarized separately) and reproductive / developmental toxicity satellite groups of 12 females per exposure level. The reproductive and developmental toxicity satellite groups were exposed for two weeks prior to breeding,

	during breeding (up to two weeks), and continuing until day 19 of gestation. Males from the main study were used to breed these females. The dams were allowed to deliver their litters, which were retained until postnatal day 4. Effects on general toxicity, gonadal function, mating behavior, implantation, and general fertility were evaluated in the satellite group adults, followed by a gross necropsy of the satellite group females on lactation day 5. Litter size, pup survival, sex, body weight, and the presence of gross external malformations was assessed in the offspring.
Results	
NOAEL (NOEL)	20 mg/L.
LOAEL (LOEL)	Not applicable.
Remarks	Actual time-weighted averages for total olefins for the 2, 10 and 20 mg/L exposure groups were **2.17** ± 0.461, **9.81** ± 1.66, **19.1** ± 2.63 mg/L, respectively, over the 37 exposure days in the study. Owing in part to the nature of the test material, there were technical difficulties in generating vapors from the test material, such that targeted exposure concentrations were not met on one entire day and for brief periods on a few other days. However, the affected instances were limited relative to the total duration of the study and were considered to have no significant impact on study integrity. There were no deaths or treatment-related clinical observations noted. No significant 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 at any dose level on any of the reproductive parameters evaluated in this study. These included measures of reproductive performance (mating, conception and fertility , time to mating, gestation length, litter size), offspring survival (gestation and postnatal survival indices, percent pre- and post-implantation loss), pup body weight and pup sex ratio. The only statistically identified change in any of these parameters was an increase in post-implantation loss occurring only at the low-dose. This was considered a spurious finding, given the lack of a dose response. Of the 12 females mated in each group, the number of viable litters produced was 11, 11, 11, and 12 for the 0, 2, 10 and 20 mg/L exposure level groups, respectively. External morphological alterations observed in the pups were limited to a hernia observed in a single pup from the high dose group. Given the low incidence of this finding, it was considered to be a spontaneous finding unrelated to exposure.
Conclusions	Repeated inhalation exposure of C4 Crude Butadiene, Low 1,3-Butadiene to male and female Sprague Dawley rats at levels of 0, 2, 10, or 20 mg/L produced no evidence of developmental toxicity or teratogenicity, as assessed in the OECD 422 study design. Based on these data, the no-observable-effect level (NOEL) for developmental toxicity was 20 mg/L, the highest

	concentration tested.
Data Quality	
Reliabilities	Klimisch value = 1 (Reliable without restrictions).
References	Carney, E.W., Liberacki, A.B., Thomas, J., Houtman, C.E. and Marable, B.R. (2001). C4 Crude butadiene, low 1,3-butadiene content: a combined repeated exposure inhalation toxicity study with the reproduction/developmental screening test in Sprague Dawley rats. Report of The Dow Chemical Company conducted for the American Chemistry Council Olefins Panel.
Other	
Last changed	6-Aug-01 Robust summary prepared by contractor to Olefins Panel

AQUATIC TOXICITY ROBUST SUMMARIES

Fish Acute Toxicity

Test Substance*:	Other TS
Method/Guideline*:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type):	Acute Fish Toxicity Calculation; LC50
GLP:	Not applicable
Year (study performed):	Not applicable
Species: **Analytical Monitoring:**	Freshwater Fish (calculated toxicity values are not species specific) Not applicable
Exposure Period:	96 hours
Statistical Method: (FT - ME)*	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPIWIN computer model (2). KOWWIN also has a database of experimental Kow values (EXPKOW.DB). The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of toxicity data for component chemicals is an estimate of the potential toxicity of category products. Chemical — Calculated log K_{ow} — Measured* log K_{ow} Isobutane — 2.23 — 2.76 n-butane — 2.31 — 2.89 isobutylene — 2.23 — 2.34 cis-butene-2 — 2.09 — 2.31 trans-butene-2 — 2.09 — 2.33 butene-1 — 2.17 — 2.40 1,3-butadiene — 2.03 — 1.99

	* Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the fish acute toxicity range of this category are C4 hydrocarbons that are common across the 10 CAS numbers (see Test Substance). Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (3). 1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92. 2. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. 3. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**	Calculated fish acute toxicity values for 7 chemicals representative of products in the Crude Butadiene C4 Category are as follows: Chemical — Calculated log K_{ow} — Fish Acute 96-hr LC50 (mg/L) Isobutane — 2.23 — 26.19 n-butane — 2.31 — 22.03 isobutylene — 2.23 — 25.28 cis-butene-2 — 2.09 — 34.23 trans-butene-2 — 2.09 — 34.23 butene-1 — 2.17 — 28.79 1,3-butadiene — 2.03 — 37.59

	Chemical / Measured* log K_{ow} / Fish Acute 96-hr LC50 (mg/L) Isobutane 2.76 8.32 n-butane 2.89 6.28 isobutylene 2.34 19.93 cis-butene-2 2.31 21.26 trans-butene-2 2.33 20.36 butene-1 2.40 17.50 1,3-butadiene 1.99 40.98 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated Kow values, products in this category are expected to have a fish 96-hour LC50 range of 22.03 to 37.59 mg/L. Based on the measured Kow values, products in this category are expected to have a fish 96-hour LC50 range of 6.28 to 40.98 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The toxicity values are calculated.
Reference: (FT - RE)	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for " acute toxicity to fish ". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext
IUCLID fields include:
- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Daphnid Acute Toxicity

Test Substance*:	Other TS
Method/Guideline*:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type): **GLP:**	Acute Daphnid Toxicity Calculation; LC50 Not applicable
Year (study performed):	Not applicable
Species:	Daphnid (calculated toxicity values are not species specific)
Analytical Monitoring:	Not applicable
Exposure Period:	48 hours
Statistical Method: (FT - ME)*	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPIWIN computer model (2). KOWWIN also has a database of experimental Kow values (EXPKOW.DB). The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of toxicity data for component chemicals is an estimate of the potential toxicity of category products. Chemical — Calculated log K_{ow} — Measured* log K_{ow} Isobutane 2.23 2.76 n-butane 2.31 2.89 isobutylene 2.23 2.34 cis-butene-2 2.09 2.31 trans-butene-2 2.09 2.33 butene-1 2.17 2.40 1,3-butadiene 2.03 1.99 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured

values.

Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4.

The seven chemicals selected to represent the daphnid acute toxicity range of this category are C4 hydrocarbons that are common across the 10 CAS numbers (see Test Substance). Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (3).

1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92.
2. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
3. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.

Results: (FT - RS)

Units/Value:

- **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

Calculated daphnid acute toxicity values for 7 chemicals representative of products in the Crude Butadiene C4 Category are as follows:

Chemical	Calculated log K_{ow}	Daphnid Acute 48-hr LC50 (mg/L)
Isobutane	2.23	28.51
n-butane	2.31	24.11
isobutylene	2.23	27.53
cis-butene-2	2.09	36.91
trans-butene-2	2.09	36.91
butene-1	2.17	31.21
1,3-butadiene	2.03	40.27

Chemical	Measured* log K_{ow}	Daphnid Acute 48-hr LC50 (mg/L)

	Isobutane 2.76 9.39 n-butane 2.89 7.15 isobutylene 2.34 21.86 cis-butene-2 2.31 23.28 trans-butene-2 2.33 22.32 butene-1 2.40 19.28 1,3-butadiene 1.99 43.88 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated Kow values, products in this category are expected to have a daphnid 48-hour LC50 range of 24.11 to 40.27 mg/L. Based on the measured Kow values, products in this category are expected to have a daphnid 48-hour LC50 range of 7.15 to 43.88 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The toxicity values are calculated.
Reference: (FT - RE)	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for " acute toxicity to aquatic invertebrates ". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Alga Toxicity

Test Substance*:	Other TS
Method/Guideline*:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type): **GLP:**	Green Alga Toxicity Calculation; EC50 Not applicable
Year (study performed):	Not applicable
Species:	Freshwater Green Alga (calculated toxicity values are not species specific)
Analytical Monitoring:	Not applicable
Exposure Period:	96 hours
Statistical Method: (FT - ME)*	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPIWIN computer model (2). KOWWIN also has a database of experimental Kow values (EXPKOW.DB). The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of toxicity data for component chemicals is an estimate of the potential toxicity of category products. Chemical — Calculated log K_{ow} — Measured* log K_{ow} Isobutane — 2.23 — 2.76 n-butane — 2.31 — 2.89 isobutylene — 2.23 — 2.34 cis-butene-2 — 2.09 — 2.31 trans-butene-2 — 2.09 — 2.33 butene-1 — 2.17 — 2.40 1,3-butadiene — 2.03 — 1.99 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more

than 13,000 organic compounds with reliably measured values..

Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4.

The seven chemicals selected to represent the alga toxicity range of this category are C4 hydrocarbons that are common across the 10 CAS numbers (see Test Substance). Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (3).

1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92.
2. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
3. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.

Results: (FT - RS)

Units/Value:

- **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

Calculated alga toxicity values for 7 chemicals representative of products in the Crude Butadiene C4 Category are as follows:

Chemical	Calculated log K_{ow}	Alga Toxicity 96-hr EC50 (mg/L)
Isobutane	2.23	18.06
n-butane	2.31	15.35
isobutylene	2.23	17.44
cis-butene-2	2.09	23.19
trans-butene-2	2.09	23.19
butene-1	2.17	19.71
1,3-butadiene	2.03	25.27

	Measured*	Alga Toxicity

	Chemical — log K_{ow} — 96-hr EC50 (mg/L) Isobutane — 2.76 — 6.13 n-butane — 2.89 — 4.71 isobutylene — 2.34 — 13.94 cis-butene-2 — 2.31 — 14.81 trans-butene-2 — 2.33 — 14.22 butene-1 — 2.40 — 12.33 1,3-butadiene — 1.99 — 27.42 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated Kow values, products in this category are expected to have an alga 96-hour EC50 range of 15.35 to 25.27 mg/L. Based on the measured Kow values, products in this category are expected to have an alga 96-hour EC50 range of 4.71 to 27.42 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The toxicity values are calculated
Reference: (FT - RE)	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "acute toxicity to aquatic plants". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext

IUCLID fields include:

- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

COURTNEY M. PRICE
VICE PRESIDENT
CHEMSTAR

May 4, 2004

American Chemistry Council *Good Chemistry Makes It Possible*

The Honorable Michael O. Leavitt
Administrator
U.S. Environmental Protection Agency
P. O. Box 1473
Merrifield, VA 22116

RE: Olefins Panel Category Report for the Crude Butadiene C4 Category
Under the HPV Challenge Program: HPV Registration No. 1101064

Dear Administrator Leavitt:

On May 4, 2000, the American Chemistry Council Olefins Panel (Panel) submitted a Test Plan under the High Production Volume (HPV) Chemical Challenge Program pertaining to the Crude Butadiene C4 Category. Robust summaries for testing and modeling studies conducted for this category were submitted to EPA on December 13, 2001 and October 14, 2003. With this letter, the Panel submits the Category summary for the Crude Butadiene C4 Category.

After all data were evaluated to determine whether the streams formed a cohesive category, it was decided that two streams should be considered as a separate category and these two streams were removed from the Crude Butadiene C4 category. A category summary report characterizing the HPV Program endpoints for these two streams will be prepared and submitted separately, later in 2004. This Category Summary reports on all remaining C4 streams (the C4 Crude Butadiene and Butadiene Unit Heavy Ends Streams). The robust summaries have been modified slightly to reflect the change in the category. The category report includes these revised robust summaries, which should replace the robust summaries previously submitted by the Panel with the Test Plan.

With the submission of this category report, the Panel has completed its obligation under the HPV Challenge Program for the Crude Butadiene C4 category.

If you have any questions, please contact Elizabeth Moran, Manager of the Olefins Panel, at 301 924 2006 or Elizabeth_Moran@americanchemistry.com.

Sincerely Yours,

Attachment

201-15092

ROBUST SUMMARIES PART 1

CRUDE BUTADIENE C4 ROBUST SUMMARIES

ARE ALSO USED FOR PYROLYSIS C3+ AND C4+

ROBUST SUMMARIES OF STUDIES USED TO CHARACTERIZE THE

CRUDE BUTADIENE C4 CATEGORY ARE ALSO USED FOR PYROLYSIS C3+ AND C4+

PHYSICO-CHEMICAL ROBUST SUMMARIES

Melting Point

Test Substance*:	Other TS
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Melting Point estimations performed by MPBPWIN are based on the average result of the calculation methods of K. Joback and Gold and Ogle. Joback's Method is described in Joback, K.G. 1982. A Unified Approach to Physical Property Estimation Using Multivariate Statistical Techniques. In The Properties of Gases and Liquids. Fourth Edition. 1987. R.C. Reid, J.M. Prausnitz and B.E. Poling, Eds. The Gold and Ogle Method simply uses the formula Tm = 0.5839Tb, where Tm is the melting point in Kelvin and Tb is the boiling point in Kelvin.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated MP (°C) / Measured* MP (°C) Isobutane: -132.55 / -138.3 n-butane: -120.28 / -138.2 isobutylene: -130.88 / -140.4 cis-butene-2: -120.41 / -105.5 trans-butene-2: -120.41 / -105.5 butene-1: -121.74 / -145.0 1,3-butadiene: -123.21 / -108.9 * Experimental values are supplied by the MPBPWIN program database (EXP_MBVP.DB) which contains more

	than 11,000 organic compounds with reliably measured values which are taken from SRC's PHYSPROP Database. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the melting range of this category are C4 hydrocarbons that are common across the 10 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated values, products in this category can have a melting range of -132.55 to -120.28 °C. Based on the measured values, products in this category can have a melting range of -145.0 to -105.5°C.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical

	structure and experimental values available in the MPBPWIN program and represent a potential melting range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. WSKOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "melting point". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Boiling Point

Test Substance*:	Other TS
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Pressure:	760 mm Hg
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Boiling Point estimations performed by MPBPWIN are based on the calculation method of S. Stein and R. Brown in "Estimation of Normal Boiling Points from Group Contributions". 1994. J. Chem. Inf. Comput. Sci. **34**: 581-587.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated BP (°C) / Measured* BP (°C) Isobutane 3.21 -11.7 n-butane 19.58 -0.5 isobutylene 10.18 -6.9 cis-butene-2 27.82 0.8 trans-butene-2 27.82 0.8 butene-1 17.57 -1.3 1,3-butadiene 15.55 -4.4 * Experimental values are supplied by the MPBPWIN program database (EXP_MBVP.DB) which contains more than 11,000 organic compounds with reliably measured values which are taken from SRC's PHYSPROP Database. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the boiling range of this category are C4 hydrocarbons that are common

	across the 10 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated values, products in this category can have a boiling range of 3.21 to 27.82 °C. Based on the measured values, products in this category can have a boiling range of -11.7 to 0.8°C.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the MPBPWIN program and represent a potential boiling point range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. WSKOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "boiling point". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Vapor Pressure

Test Substance*:	Other TS
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Vapor Pressure estimations performed by MPBPWIN are based on the average result of the calculation methods of Antoine and Grain. Both methods use boiling point for the calculation. The Antoine Method is described in the Handbook of Chemical Property Estimation. Chapter 14. W.J. Lyman, W.F. Reehl and D.H. Rosenblatt, Eds. Washington, D.C.: American Chemical Society. 1990. A modified Grain Method is described on page 31 of Neely and Blau's Environmental Exposure from Chemicals, Volume 1, CRC Press. 1985.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical — Calculated VP (hPa) — Measured* VP (hPa) Isobutane — 3.45 E^3 — 3.08 E^3 n-butane — 2.41 E^3 — 2.43 E^3 isobutylene — 2.97 E^3 — 3.08 E^3 cis-butene-2 — 2.31 E^3 — 2.33 E^3 trans-butene-2 — 2.31 E^3 — 2.33 E^3 butene-1 — 2.48 E^3 — 3.00 E^3 1,3-butadiene — 2.73 E^3 — 2.81 E^3 * Experimental values are supplied by the MPBPWIN program database (EXP_MBVP.DB) which contains more than 11,000 organic compounds with reliably measured values which are taken from SRC's PHYSPROP Database. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-

	butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the vapor pressure range of this category are C4 hydrocarbons that are common across the 10 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated values, products in this category can have a vapor pressure range of 2.31 E^3 to 3.45 E^3 hPa. Based on the measured values, products in this category can have a vapor pressure range of 2.33 E^3 to 3.08 E^3 hPa.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the MPBPWIN program and represent a potential vapor pressure range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. MPBPWIN is contained in the

	computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "vapor pressure". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:
RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Partition Coefficient

Test Substance*:	Other TS
Method/Guideline:	Calculated values using KOWWIN version 1.65, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Octanol / Water Partition Coefficient estimations performed by KOWWIN are based on an atom/fragment contribution method of W. Meylan and P. Howard in "Atom/fragment contribution method for estimating octanol-water partition coefficients". 1995. *J. Pharm. Sci.* **84**:83-92.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated log K_{ow} / Measured* log K_{ow} Isobutane 2.23 2.76 n-butane 2.31 2.89 isobutylene 2.23 2.34 cis-butene-2 2.09 2.31 trans-butene-2 2.09 2.33 butene-1 2.17 2.40 1,3-butadiene 2.03 1.99 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the partition coefficient range of this category are C4 hydrocarbons that

	are common across the 10 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated K_{ow} values, products in this category can have a partition coefficient range of 2.03 to 2.31. Based on the measured K_{ow} values, products in this category can have a partition coefficient range of 1.99 to 2.89.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include calculated values based on the chemical structure and experimental values available in the KOWWIN program and represent a potential partition coefficient range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "partition coefficient". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Water Solubility

Test Substance*:	Other TS
Method/Guideline:	Calculated values using WSKOWWIN version 1.36, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Water Solubility estimations performed by WSKOWWIN are based on a Kow correlation method described by W. Meylan, P. Howard and R. Boethling in "Improved method for estimating water solubility from octanol/water partition coefficient". *Environ. Toxicol. Chem*. **15**:100-106. 1995.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Chemical / Calculated WS (mg/L) / Measured* WS (mg/L) Isobutane 496.4 175.1 n-butane 424.1 135.6 isobutylene 495.6 399.2 cis-butene-2 652.7 423.5 trans-butene-2 652.7 407.1 butene-1 557.7 354.8 1,3-butadiene 732.4 792.3 * Experimental K_{ow} values supplied by the WSKOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the water solubility range of this category are C4 hydrocarbons that

	are common across the 10 CAS numbers. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated K_{ow} values, products in this category can have a water solubility range of 424.1 to 732.4 mg/L. Based on the measured K_{ow} values, products in this category can have a water solubility range of 135.6 to 792.3 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include values estimated using calculated K_{ow} and experimental K_{ow} values available in the WSKOWWIN program and represent a potential water solubility range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. WSKOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "water solubility". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

ENVIRONMENTAL FATE ROBUST SUMMARIES

Photodegradation (Direct)

Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Type (air, soil, water, other):	Not applicable
Light Source:	Not applicable
Light Spectrum: • **Wave length value (upper/lower)**	Not applicable
Relative Intensity:	Not applicable
Test Substance Spectrum:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol**	Not applicable
Direct Photolysis:** **Results: half-life, % degradation, quantum yield**	**Summary** In the environment, photolysis will not significantly contribute to the degradation of chemicals in the Crude Butadiene C4 Category (C4 refers to a chemical with 4 carbons). The Crude Butadiene C4 Category includes two process streams: • **C4 Crude Butadiene** • **Butadiene Unit Heavy Ends** Ten CAS numbers (see Test Substance) identify products derived from these process streams. As discussed below, the reaction process involved in direct photolysis occurs when sufficient light energy excites a molecule to the degree that a structural transformation occurs. In general, products in this

	category do not contain component chemicals that will undergo direct photolysis. **The Crude Butadiene C4 Category** A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. Process streams containing 10 to 92% butadiene are referred to as "crude butadiene." The CAS numbers or streams in this category consist of complex mixtures of hydrocarbons. Most commercial products in this category have a carbon number distribution predominantly between C3 and C5. All of these streams contain significant levels of 1,3-butadiene and olefins, which is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Crude Butadiene C4. The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process). Crude butadiene streams arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the two process streams in this category are: • **C4 Crude Butadiene** is produced by the distillation of a condensed portion of cracked gas in an ethylene process. C4 Crude Butadiene typically contains 40% to about 60% 1,3-butadiene, but could contain between 10% and 82% butadiene. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. • **Butadiene Unit Heavy Ends** is produced by extractive distillation of cracked gas. The 1,3-butadiene content of this mixed stream ranges from 13% to 92%. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. Only three companies report isolating this stream which is more typically an un-isolated intermediate.

	Photolysis of Hydrocarbons The direct photolysis of an organic molecule occurs when it absorbs sufficient light energy to result in a structural transformation (2). The reaction process is initiated when light energy in a specific wavelength range elevates a molecule to an electronically excited state. However, the excited state is competitive with various deactivation processes that can result in the return of the molecule to a non excited state. The absorption of light in the ultra violet (UV)-visible range, 110-750 nm, can result in the electronic excitation of an organic molecule. Light in this range contains energy of the same order of magnitude as covalent bond dissociation energies (2). Higher wavelengths (e.g., infrared) result only in vibrational and rotational transitions, which do not tend to produce structural changes to a molecule. The stratospheric ozone layer prevents UV light of less than 290 nm from reaching the earth's surface. Therefore, only light at wavelengths between 290 and 750 nm can result in photochemical transformations in the environment (2). Although the absorption of UV light in the 290-750 nm range is necessary, it is not always sufficient for a chemical to undergo photochemical degradation. Energy may be re-emitted from an excited molecule by mechanisms other than chemical transformation, resulting in no change to the parent molecule. A conservative approach to estimating a photochemical degradation rate is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by the molecule (3). Saturated hydrocarbons do not absorb light above 200 nm. Some characteristic absorbance maxima (λ_{max}) and associated molar absorptivities (ε) for selected unsaturated hydrocarbons are shown below (2):

	Hydrocarbon	**λ below 290 nm**	
		λ_{max}	**ε**
	Ethylene	193	10,000
	1,3-Butadiene	217	2,090
Direct Photolysis: (cont.)** **Results: half-life, % degradation, quantum yield**	Olefins with one double bond, two conjugated double bonds, or multiple un-conjugated bonds, which constitute the majority of the chemicals in the Crude Butadiene C4 Category, do not absorb appreciable light energy above 290 nm. The absorption of UV light to cause cis-trans isomerism about the double bond of an olefin occurs only if it is in conjugation with an aromatic ring (2). Products in the Crude Butadiene C4 Category do not contain component molecules that will undergo direct photolysis. Therefore, this fate process will not contribute to a measurable degradative removal of chemical components in this category from the environment. **References** 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. Virginia, USA. 2. Harris, J. C. 1982. "Rate of Aqueous Photolysis," Chapter 8 in: W. J. Lyman, W. F. Reehl, and D. H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, USA. 3. Zepp, R. G. and D. M. Cline. 1977. Rates of Direct Photolysis in the Aqueous Environment, Environ. Sci. Technol., 11:359-366.		
Indirect Photolysis:** • **Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life**	Not applicable		
Degradation Products:** • **Note: Identification, concentration**	Unknown		

Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Not applicable
Reliability: (FT - RL)	Not applicable
Reference: (FT - RE)	American Chemistry Council, Olefins Panel. 2002. Hydrolysis: Crude Butadiene C4 Category. Rosslyn, VA, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "photodegradation". Selecting this option refers the reader to information in the "freetext" field for "test substance".
** In IUCLID, provide addtional discussion if needed in the results freetext
FT - Freetext
IUCLID fields include:
- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Photodegradation (Indirect)

Test Substance*:	Other TS
Method/Guideline:	Calculated values using AOPWIN version 1.89, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Type (air, soil, water, other):	Not applicable
Light Source:	Sunlight
Light Spectrum: • **Wave length value (upper/lower)**	Natural sunlight
Relative Intensity:	1
Test Substance Spectrum:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol**	Indirect photodegradation, or atmospheric oxidation potential, is based on the structure-activity relationship methods developed by R. Atkinson. Temperature: 25°C Sensitizer: OH radical Concentration of Sensitizer: 1.5 E^6 OH radicals/cm^3
Direct Photolysis:** **Results: half-life, % degradation, quantum yield**	Not applicable
Indirect Photolysis:** • **Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life**	In the environment, organic chemicals emitted into the troposphere are degraded by several important transformation processes. The dominant transformation process for most compounds is the daylight reaction with hydroxyl (OH-) radicals (1,2). The rate at which an organic compound reacts with OH- radicals is a direct measure of its atmospheric persistence (3). AOPWIN estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The rate constants estimated by the program are then used to calculate atmospheric half-lives for organic compounds based upon

average atmospheric concentrations of hydroxyl radicals.

Since the reactions only take place in the presence of sunlight, the atmospheric half-lives are normalized for a 12-hour day.

Chemical	Calculated* half-life (hrs)	OH- Rate Constant (cm^3/molecule-sec)
Isobutane	52.6	$2.4\ E^{-12}$
n-butane	48.8	$2.6\ E^{-12}$
isobutylene	2.5	$51.7\ E^{-12}$
cis-butene-2	2.3	$56.7\ E^{-12}$
trans-butene-2	2.0	$64.3\ E^{-12}$
butene-1	4.7	$27.4\ E^{-12}$
1,3-butadiene	1.9	$66.6\ E^{-12}$

* Atmospheric half-life values are based on a 12-hr day.

Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4.

The seven chemicals selected to represent the atmospheric half-life range of this category are C4 hydrocarbons that are common across the 10 CAS numbers listed under Test Substance. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (4).

References:

1. Atkinson, R. 1988. Estimation of gas-phase hydroxyl radical rate constants for organic chemicals. *Environ. Toxicol. Chem.* **7**:435-442.
2. Atkinson, R. 1989. Kinetics and mechanisms of the gas-phase reactions of the hydroxyl radical with organic compounds. J. Phys. Chem. Ref. Data Monograph No. 1, Amer. Inst. Physics & Amer. Chem. Soc., NY.
3. Meylan, W.M. and P.H. Howard. 1993. Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. *Chemosphere* **12**:2293-2299.
4. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4

	Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Degradation Products:** • **Note: Identification, concentration**	Unknown
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Atmospheric oxidation vial hydroxyl radical can be a significant route of degradation for products in this category. Based on calculated values, products in this category can have an atmospheric half-life range of 1.9 to 52.6 hours as a result of indirect photolysis by hydroxyl radical attack.
Reliability: (FT - RL)	(2) Reliable with restrictions The results include values calculated using the AOPWIN program and represent a potential atmospheric half-life range for products with the 10 CAS numbers listed under Test Substance.
Reference: (FT - RE)	Meylan, M., SRC 1994-1999. AOPWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "photodegradation". Selecting this option refers the reader to information in the "freetext" field for "test substance".
** In IUCLID, provide additional discussion if needed in the results freetext
FT - Freetext
IUCLID fields include:
RL - Reliability
TC - Test Conditions

RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Hydrolysis (Stability in Water)

Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
Type (test type):	Not applicable
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Analytical Monitoring:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration preparation, vessel type, volume, replication, deviations from guideline or protocol**	Not applicable
Results: (FT - RS) **Units/Value:** • **Note: Analytical method, observations, half-lives by pH, degradation products**	Not applicable
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	**Summary** In the environment, hydrolysis will not contribute to the

degradation of chemicals in the Crude Butadiene C4 Category (C4 refers to a chemical with 4 carbons). This category includes two process streams:

- **C4 Crude Butadiene**
- **Butadiene Unit Heavy Ends**

Ten CAS numbers (see Test Substance) identify products derived from these process streams. As discussed below, the chemicals in these streams are composed of carbon and hydrogen and are not amenable to hydrolysis because of their molecular structure and the chemical reaction required for this type of transformation to occur.

The Crude Butadiene C4 Category

A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. Process streams containing 10 to 92% butadiene are referred to as "crude butadiene." The CAS numbers or streams in this category consist of complex mixtures of hydrocarbons.

Most commercial products in this category have a carbon number distribution predominantly between C3 and C5. All of these streams contain significant levels of 1,3-butadiene and olefins, which is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Crude Butadiene C4.

The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process).

Crude butadiene streams arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the two process streams in this category are:

- **C4 Crude Butadiene** is produced by the distillation of a condensed portion of cracked gas in an ethylene process. C4 Crude Butadiene typically contains 40% to about 60% 1,3-butadiene, but could contain between 10% and 82%

butadiene. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons.

- **Butadiene Unit Heavy Ends** is produced by extractive distillation of cracked gas. The 1,3-butadiene content of this mixed stream ranges from 13% to 92%. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. Only three companies report isolating this stream which is more typically an un-isolated intermediate.

Hydrolysis of Hydrocarbons as a Function of Molecular Structure

Hydrolysis of an organic molecule occurs when a molecule (R-X) reacts with water (H_2O) to form a new carbon-oxygen bond after the carbon-X bond is cleaved (2,3). Mechanistically, this reaction is referred to as a nucleophilic substitution reaction, where X is the leaving group being replaced by the incoming nucleophilic oxygen from the water molecule. The leaving group, X, must be a molecule other than carbon because for hydrolysis to occur, the R-X bond cannot be a carbon-carbon bond.

The carbon atom lacks sufficient electronegativity to be a good leaving group and carbon-carbon bonds are too stable (high bond energy) to be cleaved by nucleophilic substitution. Thus, hydrocarbons, including alkenes, are not subject to hydrolysis (3) and this fate process will not contribute to the degradative loss of chemical components in this category from the environment.

Under strongly acidic conditions the carbon-carbon double bond found in alkenes, such as those in the Crude Butadiene C4 Category, will react with water by an addition reaction mechanism (2). The reaction product is an alcohol. This reaction is not considered to be hydrolysis because the carbon-carbon linkage is not cleaved and because the reaction is freely reversible (3).

Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (4). The chemicals in this category are primarily olefins that contain at least one double bond (alkenes). The remaining chemicals are saturated hydrocarbons (alkanes). These two groups of chemicals contain only carbon and hydrogen. As such, their molecular structure is not subject to the hydrolytic mechanism discussed above. Therefore, chemicals in the Crude Butadiene C4 Category have a very low potential to hydrolyze, and this degradative process will not contribute to their removal in the environment.

References

	1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA. 2. Gould, E.S. (1959), Mechanism and Structure in Organic Chemistry, Holt, Reinhart and Winston, New York, NY, USA. 3. Harris, J.C. (1982), "Rate of Hydrolysis," Chapter 7 in: W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, NY, USA. 4. Neely, W. B. 1985. Hydrolysis. In: W. B. Neely and G. E. Blau, eds. Environmental Exposure from Chemicals. Vol I., pp. 157-173. CRC Press, Boca Raton, FL, USA.
Reliability: (FT - RL)	Not applicable
Reference: (FT - RE)	American Chemistry Council, Olefins Panel. 2002. Hydrolysis: Crude Butadiene C4 Category. Rosslyn, VA, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "hydrolysis". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Transport / Distribution (Fugacity)

Test Substance*:	Other TS
Method/Guideline:	Calculated according to Mackay Level I, EQC Model version 1.01
Year (guideline):	1997
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. Physical properties input into the model are those calculated by the EPIWIN Estimation v 3.04 program (1) or supplied by the databases of experimental values contained with EPIWIN. Output data from the equilibrium model provides basic information on the potential distribution of chemicals between selected environmental compartments (i.e. air, water, soil, sediment, suspended sediment, biota). 1. EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of partitioning data for component chemicals is an estimate of the partitioning behavior for category products. Calculated* Percent Distribution: Air / Water; Measured** Percent Distribution: Air / Water Isobutane: 99.99 / 0.01 / 99.99 / 0.01 n-butane: 99.98 / 0.02 / 99.99 / 0.01 isobutylene: 99.98 / 0.02 / 99.99 / 0.01 cis-butene-2: 99.97 / 0.03 / 99.98 / 0.02

	trans-butene-2 99.97 0.03 99.98 0.02 butene-1 99.98 0.02 99.99 0.01 1,3-butadiene 99.97 0.03 99.97 0.03 * Distribution values determined using input data calculated by the EPIWIN program **Distribution values determined using input data supplied by the EPIWIN program experimental databases (EXPKOW.DB, EXP_MBVP.DB, and EXP_MBVP.DB) which contain more than 11,000 organic compounds with reliably measured values. Distribution of each chemical to each remaining compartment (soil, sediment, suspended sediment, biota) was calculated as less than 0.01%. Mobility in the environment is expected to be high due to the relatively high water solubility and high vapor pressure of these chemicals. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the transport / distribution range of this category are C4 hydrocarbons that are common across the 10 CAS numbers (see Test Substance) and can represent a significant proportion of a product. Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked

	68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Products in the Crude Butadiene C4 Category are expected to distribute to air with a small percentage partitioning to water.
Reliability: (FT - RL)	(2) Reliable with restrictions The input data used to run the EQC Level I model include estimated values calculated by the EPIWIN program based on chemical structure, and experimental values supplied by the EPIWIN program databases. The partitioning data represent a potential distribution range for products with the 10 CAS numbers listed under Test Substance. Computer modeling is an accepted method of assessing environmental distribution of chemicals.
Reference: (FT - RE)	Mackay, D.A. DiGuardo, S. Paterson, and C. Cowan. EQC Model Version 1.01. 1997. Available from the Environmental Modeling Centre, Trent University, Canada.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "transport / distribution". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext

IUCLID fields include:

- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Biodegradation

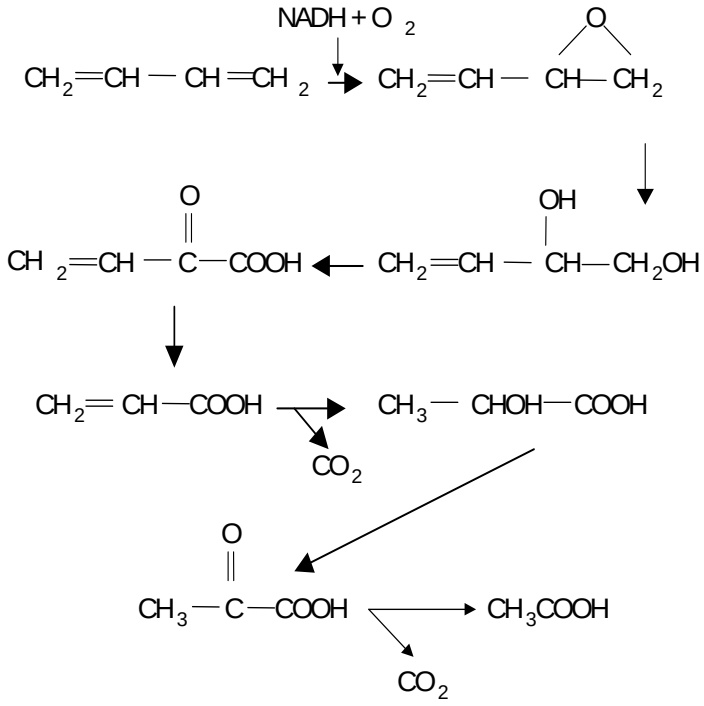
Test Substance*:	Other TS
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Inoculum:	Not applicable
Exposure Period:	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Not applicable
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Not applicable
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	**SUMMARY** In the environment, biodegradation will not contribute significantly to the loss of chemicals in products from the

	Crude Butadiene C4 Category (C4 refers to a chemical with 4 carbons). This category includes two process streams: • **C4 Crude Butadiene** • **Butadiene Unit Heavy Ends** Ten CAS numbers (see Test Substance) identify products derived from these process streams. The products contain various chemicals composed of carbon and hydrogen. As discussed below, products in this category are gaseous. If they are released to the environment, their chemical components will partition primarily to the air where they can degrade rapidly by physicochemical reactions. It is far less likely that products from this category will partition to environmental compartments where they could be degraded by bacteria. **The Crude Butadiene C4 Category** A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. Process streams containing 10 to 92% butadiene are referred to as "crude butadiene." The CAS numbers or streams in this category consist of complex mixtures of hydrocarbons. Most commercial products in this category have a carbon number distribution predominantly between C3 and C5. All of these streams contain significant levels of 1,3-butadiene and olefins, which is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated Crude Butadiene C4. The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process). Crude butadiene streams arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the three process streams in this category are: • **C4 Crude Butadiene** is produced by the distillation of a condensed portion of cracked gas in an ethylene process.

	C4 Crude Butadiene typically contains 40% to about 60% 1,3-butadiene, but could contain between 10% and 82% butadiene. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. • **Butadiene Unit Heavy Ends** is produced by extractive distillation of cracked gas. The 1,3-butadiene content of this mixed stream ranges from 13% to 92%. Other chemicals in this mixed stream are predominately chemicals containing 4 carbons. Only three companies report isolating this stream which is more typically an un-isolated intermediate. **Biodegradation of Hydrocarbons** Biodegradation is the use of a chemical by microorganisms as a source of energy and carbon. The parent chemical is broken down to simpler, smaller chemicals, which can be converted to inorganic forms such as carbon dioxide, nitrate, sulfate, and water. Products in the Crude Butadiene C4 Category are gaseous hydrocarbons, composed predominantly of chemicals with carbon numbers smaller than C5. However, the *Full-Range Butadiene Concentrates* process stream from this category, can contain hydrocarbons greater than C4. These chemicals when isolated individually are not gaseous, but relatively volatile liquids under most environmental conditions. Several hydrocarbons as well as products that are mixtures of hydrocarbons with carbon numbers greater than C4 have been shown to biodegrade. If released to the environment, biodegradation of these chemicals will occur primarily in aquatic and terrestrial habitats. There is sufficient biodegradation data on hydrocarbons in this category that are greater than C4 to show that these chemicals have a potential to biodegrade to a great extent and not persist in the environment (see the *C5 Noncyclics, Low Benzene Naphtha, and High Benzene Naphtha* HPV Chemical Program test plans from the Olefins Panel of the American Chemistry Council, for specific data and a more detailed discussion of the biodegradability of selected hydrocarbons greater than C4.) The larger proportion of chemicals from this category are gaseous. Consequently, their availability to microbial degraders will be significantly limited. Component chemicals from all three process streams in this category are simple hydrocarbons, the majority of which will partition primarily to the air where physical processes will contribute to their degradation [see the atmospheric oxidation potential (AOP) data (as mediated by hydroxyl radical

attack) for specific degradation rates of selected chemicals from this category; AOP data were developed for this category under the HPV Chemical Program]. All chemicals from this category that partition to the air are calculated to degrade rapidly due to physical processes and not persist. Because of the partitioning behavior of chemicals in this category, biodegradative processes will be less likely to contribute to their loss from the environment.

Products from the Crude Butadiene C4 Category do not lend themselves to being evaluated for biodegradability using standard experimental techniques because of their physical state. However, there is microbial metabolism information for one of the major chemicals, 1,3-butadiene, in this category that demonstrates that it can be biodegraded. Experimental studies to determine a catabolic pathway for 1,3-butadiene as mediated by a *Nocardia* sp. (3) resulted in the following proposed series of reactions:



The intermediary metabolic steps depicted above result in the production of acetic acid, CH3COOH, which can be further metabolized. In addition, 1,3-butadiene has been estimated to have an aerobic aquatic biodegradation half-life ranging from 1 to 4 weeks (2).

The potential biodegradability of some of the higher molecular weight components including benzene, toluene, xylene, ethylbenzene, and naphthalene has been summarized

	and metabolic pathways leading to their biodegradation have been described (4). These compounds have been shown to biodegrade to high extents such that if they were to partition to either a terrestrial or aqueous environment, they would be subject to biodegradative processes that would result in their removal from the environment. In summary, because the C4 and lighter chemical components of this category will partition to the air, physical degradative processes will dominate their fate. Data show that these chemicals are subject to rapid physical degradation. Chemical components of this category that are greater than C4 also have a potential to partition to the air to a great extent, where they will also degrade rapidly in a similar manner. However, they also have a potential to partition to aquatic and terrestrial environments where they are subject to biological processes that can result in their rapid biodegradation. Overall, products from this category and their component chemicals are expected to degrade rapidly in the environment and not persist. **References** 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. Virginia, USA. 2. Howard, P.H., R.S. Boethling, W.F. Jarvis, W.M. Meylan, and E.M. Michalenko. 1991. Handbook of Environmental Degradation Rates. H.T. Printup Ed. Lewis Publishers, Chelsea, MI, USA. 3. Watkinson, R.J. and H.J. Somerville. 1976. The Microbial Utilization of Butadiene. Shell Research Limited, Sittingbourne Research Centre, Kent, UK. 4. van Agteren, M.H., S. Keuning, and D.B. Janssen. 1998. Handbook on Biodegradation and Biological Treatment of Hazardous Organic Compounds. Kluwer Academic Publishers. Boston, CT, USA.
Reliability: (FT - RL)	Not applicable
Reference: (FT - RE)	American Chemistry Council, Olefins Panel. 2002. Hydrolysis: Crude Butadiene C4 Category. Rosslyn, VA, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "biodegradation". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext

IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

HUMAN HEALTH ROBUST SUMMARIES

Acute Toxicity

Test Substance	
Remarks	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	OECD 402.
Type (test type)	Acute inhalation.
GLP	Yes.
Year	1982.
Species/Strain	Rat/Fischer 344.
Sex	Males and females.
No. of animals per sex per dose	5/sex.
Vehicle	Not applicable.
Route of administration	Inhalation (gas).
Test Conditions	A group of ten rats (age: 12 weeks, weight: 143-234 grams) were exposed to 5,300 mg/m3 (2,331 ppm) of the test substance in air for four hours. Analytical chamber concentrations were determined by gas chromatography every 15 minutes during the exposure; a single particle size sample was taken to show the absence of aerosol. Body weights were recorded prior to exposure and 7 and 14 days post-exposure. Individual clinical observations were recorded pre-exposure and daily for 14 days post-exposure. The rats were sacrificed on the fourteenth day and a gross necropsy performed.
Results	
LC50	Rat LC50 (4 hour) = >5,300 mg/m3 (2,331 ppm)
Remarks	Observations noted following exposure were two male rats with respiratory sounds/wheezing or hyperexcitability and one female with minimal porphyrin around the eyes. All rats were normal from Days 2-14. No significant necropsy findings were reported, except one female with an ovary filled with red fluid. Body weight gains appeared normal.
Conclusions	
(study author)	No mortality or significant adverse effects were observed in rats exposed to 5,300 mg/m3 (2,331 ppm) of the test substance.
Data Quality	
Reliability	Reliable without restrictions. Guideline study.
References	Gulf Oil Chemicals Company (1982). Acute LC50 Inhalation Toxicity Test in Rats with Butadiene Feedstock. Unpublished

	report (Project #82-060).
Other	Robust Summary prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	19-Oct-99

Acute Toxicity

Test Substance	1,3-butadiene CAS# 106-99-0
Method	
Method/guideline followed	Other.
Type (test type)	Acute inhalation.
GLP	Pre-GLP.
Year	1969.
Species/Strain	Rat and mouse (strains not specified).
Sex	Not specified.
No. of animals per sex per dose	Not specified.
Vehicle	Not applicable.
Route of administration	Inhalation (gas).
Test Conditions	Age, number, and sex of test animals not specified. Number of groups and exposure concentrations not specified. Dynamic flow exposure system; no description of exposure chambers or conditions. Rats exposed four hours; mice exposed two hours. No post-exposure observation period - mortality study only. Exposure concentrations "controlled" by gas chromatography.
Results	
LC50 with confidence limits	Rat LC50 (4 hour) = 285 mg/L (219-370 mg/L $p \leq 0.05$) Mouse LC50 (2 hour) = 270 mg/L (251-290 mg/L $p \leq 0.05$)
Remarks	No clinical observations or necropsy findings reported. Objective of study was to determine hydrocarbon concentrations in various tissues at lethal exposure concentrations.
Conclusions	
(study author)	LC50 value reported to be 285 mg/L (129,000 ppm) in rats, 270 mg/L (122,000 ppm) in mice.
Data Quality	
Reliability	Not assignable. Lethality study only; insufficient experimental detail to assess quality.
References	Shugaev, B.B. (1969) Concentrations of Hydrocarbons in Tissues as a Measure of Toxicity. Arch. Environ. Health 18:878-882.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	13-Oct-99

Acute Toxicity

Test Substance	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 67% 1,3-butadiene, 30% butenes, 2% 1,2-butadiene
Method	
Method/guideline followed	Other.
Type (test type)	Irritation screen in rabbits.
GLP	Yes.
Year	1985.
Species/Strain	Rabbit (New Zealand White).
Sex	1 male, 1 female.
Vehicle	Not applicable.
Route of administration	Eye and skin.
Remarks For Test Conditions	Two young adult rabbits were evaluated for eye and skin irritation. The test substance was dispensed immediately prior to dosing into a flask packed in dry ice. On the first treatment day, 0.1mL of the test substance was instilled into one eye of each rabbit. Irritation was scored at 24, 48, and 72 hours. The untreated eye served as the control. Twenty-four hours after treatment of the eye, 0.1mL of the test substance was applied to the skin of the rabbits and occluded with a rubber dam. The test sites were evaluated 1, 3, and 7 days after dosing.
Results	
Remarks	The eye irritation scores were 0 at all observation intervals. The treated skin sites were virtually free of irritation at all observation intervals.
Conclusions	
(study author)	The test substance is estimated not to be irritating to the eye or skin.
Data Quality	
Reliability	Reliable with restrictions. Screening study.
References	Mobil Environmental and Health Sciences Laboratory (1985). Irritation Screen of Butadiene Concentrate in Albino Rabbits, Unpublished report (Study No. 41652).
Other	Robust Summary prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	24-Oct-99

Genetic Toxicity - *in vitro*

Test Substance	
Test substance	1,3-butadiene CAS# 106-99-0
Method	
Method/guideline followed	No data.
Type	Reverse mutation assay (Ames *Salmonella* test).
System of testing	Bacterial.
GLP	No data.
Year	1990.
Species/Strain	Salmonella typhimurium/TA97, TA98, TA100, TA1535.
Metabolic activation	With and without.
Species and cell type	Rat, mouse, and human liver S9 fraction.
Quantity	0.8 and 4.0 mg protein/plate.
Induced or not induced	Arochlor 1254-induced and uninduced rat, mouse, and human S9.
Concentrations tested	0, 30, 40, 50, and 60% butadiene in air.
Statistical Methods	Not specified.
Remarks for Test Conditions	Concentrations of butadiene gas were metered into specially constructed treatment chambers holding the agar plates overlaid with the bacteria and activation system. Actual gas concentrations were determined by gas chromatography before and after the 48 hour exposure period. Different treatment chambers were used for each activation system and for the non-activated treatment. S9 preparations were made according to the procedure of Ames *et al.* (1975).
Results	1,3-Butadiene (BD) induced revertants only in strain TA1535. Mouse S9 showed slightly higher activity than the uninduced rat or human S9 at 30% 1,3-butadiene in air. At concentrations greater than 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 treatments. Arochlor 1254-induced rat S9 gave similar results as mouse S9 (uninduced). Since the response was weak, the S9 concentration was increased from 0.8 mg/plate to 4.0 mg/plate. Increasing the concentration of Arochlor 1254-induced rat S9 had no effect on the number of revertants; slightly more revertants were observed using 4.0 than 0.8 mg/plate of uninduced rat S9.
Conclusions	
(study author)	*Salmonella typhimurium* reverse gene mutation (Ames) tests of 1,3-butadiene using strains TA1535, TA97, TA98, and TA100 and employing rat, mouse, and human liver S9 metabolic systems were barely 2-fold above background only in strain TA1535 at 30% butadiene in air with induced and uninduced rat S9 and mouse S9 (uninduced). In general, 1,3-butadiene was a weak *in vitro* genotoxin.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study.
Reference	Arce G.T., Vincent D.R., Cunningham M..J, Choy W.N., and Sarrif

	A.M. (1990). *In vitro* and *in vivo* genotoxicity of 1,3-butadiene and metabolites. Environ. Health Perspect. 86:75-8.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	18-Oct-99

Genetic Toxicity - *in vitro*

Test Substance	
Test substance	Butadiene Concentrate, CAS# 68955-28-2. Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	OECD 482.
Type	Unscheduled DNA Synthesis (UDS).
System of testing	Primary hepatocytes derived from Fischer 344 rats.
GLP	Yes.
Year	1984.
Metabolic activation	No.
Concentrations tested	0, 1000, 5000, 10000, and 20000 ppm.
Control groups and treatment	Negative = air only; positive = 2-acetylaminofluorene (0.2ug/mL).
Statistical Methods	Group means and standard deviations for number of viable cells and nuclear grain counts. The test substance was considered positive if the mean nuclear grain count exceeded the negative control by at least 6 grains per nucleus and the negative control did not exceed 5.
Remarks for Test Conditions	Primary hepatocytes were derived from freshly perfused rat liver (1 male, 10 weeks age, 226 grams body weight). Cultures were seeded with approximately 10^5 cells/mL on Day 1. Three cultures per group were exposed to ^{3}H-thymidine and the test substance for 18-20 hours. The culture flasks were placed in sealed dessicator jars for the exposure period, and the test substance added by injection via a 50cc syringe. Cells growing on coverslips were fixed on Day 2. On Day 3 the slides were dipped in autoradiograph emulsion and stored in the dark at 2-8^{o}C. The autoradiographs were developed and stained on Day 21.
Results	A separate range-finding study was conducted to establish levels of cytotoxicity based on relative cell viability. The test substance was toxic to primary hepatocytes at 10000 ppm where 64% relative viability was observed following 18 hour exposure. At 20000 ppm, the relative viability was 57%. In the UDS study, both positive and negative control groups gave expected responses. A weak positive response was observed at 20000 ppm (7.74 nuclear grain counts vs. 1.24 in the air control vs. 107.13 in the positive control). The 1000, 5000, and 10000 ppm groups were also slightly increased (4.29-5.14) from the air control but less than the criteria for a significant response.
Conclusions	
(study author)	Cytotoxicity was observed at 10000 ppm. Increased unscheduled DNA synthesis was observed at 20000 ppm.
Data Quality	
Reliabilities	Reliable without restrictions. Guideline study.
Reference	Gulf Oil Chemicals Company (1984). Hepatocyte Primary Culture/DNA Repair Test of Butadiene Feedstock, Unpublished report (Project# 2073).

Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
L*ast changed*	18-Oct-99

Genetic Toxicity - *in vitro*

Test Substance	
Test substance	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
*Method/*guideline followed	Other.
Type	Mammalian cell transformation test.
System of testing	BALB/3T3-A31-1-1 cells.
GLP	Yes.
Year	1983.
Metabolic activation	No.
Concentrations tested	0, 1000, 5000, 10000, and 20000 ppm.
Control groups and treatment	Negative = air only; positive = 3-methylcholanthrene (1.0 ug/mL).
Statistical Methods	Group means and standard deviations for number of viable cells, cloning efficiency, and transformed foci per culture. The test substance was considered positive if there was a two-fold increase in foci compared to the negative control group.
Remarks for Test Conditions	Each treatment group consisted of 12 flask cultures for cell transformation seeded with 10000 cells and 2 plate cultures for cloning efficiency with 250 cells. The cultures were placed in sealed dessicator jars and exposed to the test substance for two days. The test substance was added to the jars by injection via a 50cc syringe and samples of the exposure atmosphere were analyzed by gas chromatography. The mediums were changed on Day 4 and then weekly. Plate cultures were fixed and stained on Day 8 and flask cultures on Day 29. Foci in transformation cultures were counted and examined microscopically to determine type.
Results	Cloning efficiency was used as a measure of toxicity under culture conditions. Toxicity was observed at 5000 ppm where a relative cloning efficiency of 53.8% was observed. The negative and positive control gave expected responses for transformation. The response for the test substance was not increased from the negative control group at any level tested.
Conclusions	
(study author)	The test substance was negative for cell transformation.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to draft OECD guideline.
Reference	Gulf Oil Chemicals Company (1983). BALB/3T3 Transformation Test Using Butadiene Feedstock, Unpublished report (Project# 2074).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	18-Oct-99

Genetic Toxicity - *in vitro*

Test Substance	
Remarks	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 67% 1,3-butadiene, 30% butenes, 2% 1,2-butadiene.
Method	
Method/guideline followed	No data.
Type	Reverse mutation assay (Ames *Salmonella* test).
System of testing	Bacterial.
GLP	Yes.
Year	1985.
Species/Strain	Salmonella typhimurium/ TA98, TA100, TA1535, TA1537, TA1538.
Metabolic activation	With and without.
Species and cell type	Rat liver S9 fraction.
Quantity	0.6 mL.
Induced or not induced	Arochlor 1254-induced.
Concentrations tested	25, 50, 75, or 100 uL.
Statistical Methods	The test substance was considered mutagenic if it produced a dose-related two-fold increase in mean revertant value compared to the negative control.
Remarks for Test Conditions	The test substance was stored in a dry ice/ethanol slurry to prevent loss of volatile components and dosed by microdispenser into sterile septa-capped culture tubes. Sodium phophate buffer or S-9/bacteria mix was injected through the septa into the tubes containing the test substance and pre-incubated for 20 minutes at 37^{o}C. After the pre-incubation period, the contents of the tubes were overlayed on agar and incubated for 48 hours at 37^{o}C. Revertant colonies were counted by automatic colony counter. Positive control chemicals were: 2.0 ug 2-aminoanthracene, 15.0 ug 9-aminoacridine, 20.0 ug 2-nitrofluorene, and 5.0 ug N-methyl-N-nitro-N-nitrosoguanidine, in 50 µl DMSO per plate.
Results	A preliminary toxicity/initial mutagenicity assay was conducted over a range of 10 to 500 µl per plate in two strains (TA100 and TA1537) with and without S-9. Toxicity was exhibited at $\geq$75uL in TA100, and $\geq$100uL in TA1537. Some inconsistencies in toxicity with increasing dose level were noted that were attributed to the volatility of the test substance. Based on the toxicity data, the test substance was tested in the pre-incubation mutagenicity assay at volumes of 25, 50, 75, and 100 µl per plate. None of the five strains with or without induced rat liver S-9 exhibited reversion frequencies substantially different from spontaneous controls in this assay.
Conclusions	
(study author)	The test substance was not considered a mutagen with or without metabolic activation in this test system.

Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study.
Reference	Mobil Environmental and Health Sciences Laboratory (1985). An Ames Salmonella/Mammalian Microsome Mutagenesis Assay For Determination of Potential Mutagenicity of Butadiene Concentrate, Unpublished report (Study No. 41653).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	24-Oct-99

Genetic Toxicity - i*n vitro*

Test Substance	
Remarks	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 67% 1,3-butadiene, 30% butenes, 2% 1,2-butadiene.
Method	
Method/guideline followed	Other.
Type	Mouse lymphoma mutagenesis assay.
System of testing	Mammalian cell.
GLP	Yes.
Year	1985.
Species/Strain	Mouse lymphoma cells/ L5178Y (TK+/-; subclone 3.7.2C).
Metabolic activation	With and without.
Species and cell type	Rat liver S9 fraction.
Quantity	4.0 mL.
Induced or not induced	Arochlor 1242/1254-induced.
Concentrations tested	Nonactivated assays: 10.0, 12.5, 15.0, 17.5, 20.0, 22.5, 25.0, 27.5, 30.0, 35.0 40.0, or 45.0 uL/mL media. S-9 activated assays: 2.5, 5.0, 7.5, 10.0, 12.5, 15.0, 17.5, 20.0, 22.5, or 25.0 uL/mL.
Statistical Methods	The test substance was considered mutagenic if it produced a dose-related or toxicity-related two-fold increase in average mutant frequency compared to the negative controls, at concentrations exhibiting acceptable total growths (10% or greater).
Remarks for Test Conditions	The positive control chemical for the S-9 activated assays was 7, 12-dimethylbenz[a]anthracene (DMBA) at 2.5 and 5.0 ug/mL, and ethylmethane sulfonate (EMS) for the nonactivated assays at 0.5 and 1.0 uL/mL. An initial toxicity assay was performed with and without activation at concentrations ranging from 10 to 100 uL/mL. The dosing regimen for the mutagenesis assay was designed to produce 10-90% lethality. Six mLs of cell suspension (10^6 cells/mL) were exposed for 3 hours to the test or positive control substances. An expression period of 2 days followed with determinations of cell population densities and growth. Cultures selected for mutant analysis and cloning efficiencies were incubated for 10-12 days.
Results	Without activation, mutant frequencies and total number of mutants were significantly increased at the two highest concentrations (20.0 and 22.5 uL/mL). Although total growth was very low (5.1% and 5.5%), these levels were considered mutagenic since there was no reduction in cloning efficiency. There were no significant differences in mutant frequency for the S-9 activated cultures.
Conclusions	
(study author)	The test substance induced a significant increase in mutant frequency of mouse lymphoma cells without metabolic activation, but was evaluated as non-mutagenic in the presence of S-9 activation.

Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study.
Reference	Mobil Environmental and Health Sciences Laboratory (1985). Evaluation of the Mutagenic Potential of Butadiene Concentrate in the Mouse Lyphoma (L5178Y/TK+/-) Mutagenesis Assay, Unpublished report (Study No. 41654).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	24-Oct-99

Genetic Toxicity - i*n vivo*

Test Substance	
Remarks	1,3-butadiene CAS# 106-99-0
Method	
Method/guideline followed	Other.
Type	Mammalian erythrocyte micronucleus assay.
GLP	No data.
Year	1994.
Species	Rat and mouse.
Strain	Rat: Wistar. Mouse: CB6F1
Sex	Rat: Male. Mouse: Female.
Route of administration	Inhalation (gas).
Doses/concentration levels	0, 50, 200, or 500 ppm.
Exposure period	6 hours/day for 5 days.
Statistical methods	Student's two-tailed t-test for differences between groups.
Remarks for Test Conditions.	Twenty female CB6F1 mice (approximately 25g, 8-10 weeks old) and ten male Wistar rats (300-350g, 10 weeks old) per group were exposed for 5 days, 6 h/day 0, 50, 200, or 500 ppm of 1,3-butadiene (BD) by inhalation. An additional high concentration group of mice was exposed to 1300 ppm. Exposure concentrations were monitored by infrared spectroscopy (rats) and gas chromatography (mice). The animals were sacrificed 1 day after the last exposure and smears of blood and bone marrow erythrocytes were prepared and stained.
Results	In the rats, no effects on micronuclei frequencies were observed either in the peripheral blood or bone marrow at all exposure levels. A slight toxic effect in rat bone marrow cells (decreased polychromatic/normochromatic ratio) was observed at the 500 ppm level. In the mice, a clear dose-dependent increase in micronuclei frequency was observed in both blood and bone marrow cells at all exposure levels tested.
Conclusions	
(study author)	1,3-butadiene was active in inducing micronuclei in peripheral blood and bone marrow erythrocytes in mice at levels $\geq$50 ppm, but not in rats. The genotoxic effects observed in this study parallel the species differences observed in cancer studies.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study.
References	Autio, K., Renzi, L., Catalan, J., Albrecht, O.E., and Sorsa, M. (1994). Induction of Micronuclei in Peripheral Blood and Bone Marrow Erythrocytes of Rats and Mice Exposed to 1,3-Butadiene by Inhalation. Mut. Res. 309:315-320.
	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	25-Oct-99

Genetic Toxicity - i*n vivo*

Test Substance	
Remarks	Butadiene Concentrate, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	OECD 474
Type	Mammalian erythrocyte micronucleus test
GLP	Yes
Year	1984
Species	Mouse
Strain	Crl:CD-1 BR Swiss
Sex	Male and female
Route of administration	Inhalation (gas)
Doses/concentration levels	10,780; 20,671; 35,430 ppm
Exposure period	2 hours/day for 2 consecutive days
No. of animals per dose	10/sex/group
Control groups and treatment	10/sex negative (air) control; 5/sex positive control (cyclophosphamide, 75 mg/kg intraperitoneal injection)
Statistical methods	Group mean body weights, total polychromatic erythrocytes (PCEs), normochromatic erythrocytes (NORMs), PCEs with micronuclei, and NORMs with micronuclei were compared by t-test ($p<0.05$ = positive).
Remarks for Test Conditions.	Mice were 11 weeks old and 25-42 grams weight at study initiation. Test and control substances were administered on Days 1 and 2. Exposure concentrations determined by gas chromatography. Animals were observed daily and body weights were recorded on Days 1, 3, and 4. Five mice/sex/group were sacrificed on Days 3 and 4 and bone marrow smears prepared; positive controls (5/sex) were sacrificed on Day 3 only.
Results	No mice died during the study; the only clinical observations were an apparent unconsciousness during exposure. There were no significant body weight differences. The negative and positive control groups produced negative and positive resulats, respectively. Mice in the exposed groups showed increased micronuclei formation at all levels in both sexes. Females were statistically increased from control at all levels on Day 3 and at 20,671 ppm and 35,430 ppm on Day 4; males were significantly increased only at 35,430 ppm on both days. There was no significant change in the PCE/NORM ratio in any group.
Conclusions	
(study author)	The test material produced an increased frequency of micronucleated erythrocytes in the bone marrow of mice at all levels tested.
Data Quality	
Reliabilities	Reliable without restrictions. Guideline study.
References	Gulf Oil Chemicals Company (1984). Micronucleus Test in Mouse Bone Marrow: Butadiene Feedstock Administered by

	Inhalation For 2 Hours/Day For 2 Days, Unpublished report (Project #2014).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	13-Oct-99

Repeated Dose Toxicity

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Rubber grade, containing 0.02% t-butyl catechol; purity ≥98.94%.
Method	
Method/guideline followed	Other
Test type	14-week inhalation study
GLP	Yes
Year	1977
Species	Mouse
Strain	B6C3F1
Route of administration	Inhalation (gas)
Duration of test	14 weeks
Doses/concentration levels	0, 625, 1250, 2500, 5000, or 8000 ppm
Sex	10 male, 10 female per group
Exposure period	6 hours/day
Frequency of treatment	5 days/week, total of 63 or 64 exposures
Control group and treatment	10 male, 10 female, air-only exposed
Post exposure observation period	Not applicable
Statistical methods	Group means and standard deviations calculated for body weights.
Test Conditions	Groups of 10 mice/sex /group (4-5 weeks age at study initiation) were exposed to various levels of 1,3-butadiene for 6 hrs/day, 5 days/week for 14 weeks (64 exposures). Because four male mice in the high exposure group died by day 4, another 2 groups of 10 male mice each were restarted (control and 8000 ppm). Mice were observed once daily for morbidity and mortality; moribund animals were sacrificed. Body weights were recorded weekly. At the end of the 95 or 93-day (restart) studies, surviving mice were sacrificed. Necropsies were performed and tissues preserved. Histopathologic examinations were performed on all controls, high exposure (8000 ppm), and early deaths.
Results	
NOAEL (NOEL)	1250 ppm.
LOAEL (LOEL)	2500 ppm, based on reduced body weight gains.
Remarks	Six of ten males and 1/10 females exposed at 8000 ppm, 6/10 males and 1/10 females at 5000 ppm, and 1/10 males at 2500 or 1250 ppm died prior to study termination or were sacrificed in a moribund condition. Body weight gains were decreased in males at 2500, 5000, and 8000 ppm, and at 5000 and 8000 ppm in the females. No exposure-related histopathologic effects were observed in the high (8000 ppm) group.
Conclusions	Based on the results of this study, exposure levels of 625 and 1250 ppm were selected for a 2-year carcinogenicity study in

	mice based on reduced body weight gains and mortality in higher exposure groups.
Data Quality	
Reliabilities	Reliable with restrictions. Acceptable, well-documented study report but deficient by current guidelines. No organ weights, hematology or clinical chemistry evaluations were performed.
References	National Toxicology Program, Toxicology and Carcinogenesis Studies of 1,3-Butadiene (CAS No. 106-99-0) in B6C3F1 Mice (Inhalation Studies), NTP Technical Report Series No. 288, NIH Publication 84-2544 (1984).
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	8-Dec-99

Repeated Dose Toxicity

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity >99.2%, containing 120 ppm t-butyl catechol.
Method	
Method/guideline followed	Other.
Test type	13-week inhalation study.
GLP	No data.
Year	1977.
Species	Rat.
Strain	CD (Sprague-Dawley).
Route of administration	Inhalation (gas).
Duration of test	14 weeks.
Doses/concentration levels	0, 1000, 2000, 4000, or 8000 ppm.
Sex	40 male, 40 female per group.
Exposure period	6 hours/day.
Frequency of treatment	5 days/week for 13 weeks.
Control group and treatment	40 male, 40 female, exposed to filtered air only.
Post exposure observation period	Not applicable.
Statistical methods	Analysis of variance for body weights, food consumption, urinalysis, hematology, clinical chemistry, organ weights.
Test Conditions	Groups of 40 rats/sex /group (approx. 5 weeks age at study initiation) were exposed to various levels of 1,3-butadiene for 6 hrs/day, 5 days/week for 13 weeks. All animals were observed daily; individual body weights and food consumption were recorded weekly. Interim sacrifices of 10 rats/sex/group were performed after 2 and 6 weeks of exposure. Three urine samples were obtained from each animal during the 1-2 weeks prior to sacrifice. Blood samples were collected from all rats prior to the 2, 6, and 13 week sacrifices. Brain cholinesterase activity was measured using half the brain of 5 rats/sex/group at the 2 and 6-week sacrifices and all rats at the terminal sacrifice. Organ weights were recorded for the adrenals, brain, gonads, heart, kidneys, liver, lung, pituitary, spleen, and thyroid. Necropsies were performed and tissues preserved. Histopathologic examinations were performed on all control and high exposure (8000 ppm) tissues.
Results	
NOAEL (NOEL)	8000 ppm.
LOAEL (LOEL)	>8000 ppm.
Remarks	Increased salivation was observed in the females after 8 weeks exposure and decreased grooming (stained fur) in the males after 10 weeks. No other exposure-related conditions were observed. Male rats showed slight (non-statistically significant) reductions in body weight gains compared to the controls; female body weights at 1000 and 4000 ppm were statistically higher than the controls.

	Neuromuscular function tests using a modified rotating cone gave some random group differences, but were not considered exposure-related. There were no toxicologically significant differences in hematology, blood chemistry, brain cholinesterase measurements, or urine analysis. Organ weight and organ to brain weight ratios showed some scattered statistically significant differences among the groups but did not indicate any treatment-related effects. Microscopic examination of the tissues of the exposed rats showed a similar incidence and severity of histopathologic findings to the control group.
Conclusions	
(study author)	Rats exposed to butadiene gas at concentrations up to 8000 ppm showed no significant effects related to exposure.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study.
References	Crouch, C.N., Pullinger, D.H., and Gaunt, I.F. (1979) Inhalation Toxicity Studies With 1,3-butadiene - 2. 3 Month Toxicity Study in Rats. Am. Ind. Hyg. Assoc. J. 40:796-802.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	18-Oct-99

Repeated Dose Toxicity

Test Substance	
Remarks	Butadiene feedstock, CAS# 68955-28-2 Gases (petroleum) light steam-cracked, butadiene conc. Approximately 45% 1,3-butadiene, 20% butanes, and 30% butenes.
Method	
Method/guideline followed	Other.
Test type	9-day inhalation study.
GLP	Yes
Year	1982
Species	Rat
Strain	Fischer 344
Route of administration	Inhalation (gas)
Duration of test	12 days (9 exposures)
Doses/concentration levels	0, 2500, and 25100 mg/m3 (0, 1110, and 11140 ppm)
Sex	5 male, 5 female per group.
Exposure period	6 hours/day.
Frequency of treatment	9 exposure days
Control group and treatment	5 male, 5 female, exposed to air only.
Post exposure observation period	Not applicable.
Statistical methods	Bartlett's test and analysis of variance for body and organ weights. If the Bartlett's test indicated homogeneity, Dunnett's test was also performed; if non-homogeneous, a modified t-test was done.
Remarks for Test Conditions	Three groups of 5 rats/sex /group (8 weeks age and 120-198 grams at study initiation) were exposed to 0, 2500, or 25100 mg/m3 of the test substance for 6 hrs/day for a total of 9 exposures. The exposure regimen was 5 days of exposure , 2 days off, 4 days of exposure, then one day for the terminal sacrifice (12 days). Analytical chamber concentrations were determined by gas chromatography, 5 to 16 times per day in the low and high exposure chambers or approximately every 1.5 hours for the control chamber. A particle size sample was performed once daily for each exposure chamber to confirm the absence of aerosol. Individual animal observations were performed twice daily on exposure days and once daily on non-exposure days. Body weights were recorded prior to the first exposure and on Days 1, 7, and 12. Blood samples were obtained from all rats prior to sacrifice on Day 12. A gross necropsy was performed and organ weights recorded for the brain, heart, kidneys, liver, lung, and spleen. These organs plus the testes and ovaries were preserved and examined microscopically.
Results	
NOAEL (NOEL)	11140 ppm
LOAEL (LOEL)	>11140 ppm
Remarks	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 statistically significant 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 and tissues examined.
Conclusions	
(study author)	The 9-day repeated inhalation exposure of up to 11140 ppm (25100 mg/m3) resulted in no significant adverse effects in rats.
Data Quality	
Reliabilities	Reliable without restrictions. Comparable to guideline study (OECD 412).
References	Gulf Oil Chemicals Company (1983). Nine-day Repeated Dose Inhalation Study in Rats Using Butadiene Feedstock, Unpublished report (Project #82-090). (1983). Gulf Life Sciences Center, Pittsburgh PA
Other	Robust summary prepared by ExxonMobil Biomedical Sciences, Inc.
Last changed	19-Oct-99

Developmental Toxicity/Teratogenicity

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity 99.88%
Method	
Method/guideline followed	OECD 414.
Test type	Developmental toxicity (teratogenicity) study.
GLP	Yes.
Year	1987.
Species	Mouse.
Strain	CD-1 (Swiss).
Route of administration	Inhalation (gas).
Concentration levels	0, 40, 200, or 1000 ppm.
Sex	18-22 pregnant females per group.
Exposure period	Days 6-15 of gestation.
Frequency of treatment	6 hours/day.
Control group and treatment	Air-exposed only.
Duration of test	Females sacrificed on gestation day 18.
Statistical methods	Analysis of variance for body weights, number of resorptions, implants, live, dead or affected fetuses per litter. Significant differences among the groups were also analyzed by Duncan's multiple range test or arcsin transformation of the response proportion. Binary-response variables were between groups were compared using chi-square or Fisher's exact test.
Remarks for Test Conditions.	Female mice were mated to unexposed males and exposed from days 6-15 of gestation to 0, 40, 200, or 1000 ppm of the test substance. Analytical chamber concentrations were measured by on-line gas chromatography. Body weights were recorded on gestation days 0, 6, 11, 16, and 18. Maternal animals were observed daily for mortality, morbidity, and signs of toxicity and examined for gross tissue abnormalities at necropsy (day 18). The uterus and placenta was removed and weighed; the number of implantation sites, resorptions, live and dead fetuses were recorded. Live fetuses were weighed and subjected to external, visceral, and skeletal examinations. Approximately 50% of the fetal heads were sectioned and examined.
Results	
NOAEL maternal toxicity	40 ppm.
NOAEL developmental	40 ppm.
toxicity	There were decreases in maternal body weight gains in the 200 and 1000 ppm groups. Fetal weights were significantly reduced in both males and females at 200 and 1000 ppm; placenta weights were significantly reduced for corresponding male fetuses at 200 ppm and for 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 sternebrae) at 200 and 1000 ppm.
Conclusions	

(study author)	Developmental toxicity was observed in mice in the presence of maternal toxicity at 200 and 1000 ppm. A slight statistically significant decrease in male fetal weight (95% of control) was also observed, but the biological significance of this finding has been questioned.
Data Quality	
Reliabilities	Reliable without restrictions. Guideline study.
References	Morrissey, R.E., Schwetz, B.A., Hackett, P.L., Sikov, M.R., Hardin, B.D., McClanahan, B.J., Decker, J.R., and Mast, T.J. (1990). Overview of Reproductive and Developmental Toxicity Studies of 1,3-Butadiene in Rodents. Environ. Health Perspect. 86:79-84.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Las*t changed*	20-Oct-99

Developmental Toxicity/Teratogenicity

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity 99.88%
Method	
Method/guideline followed	OECD 414.
Test type	Developmental toxicity (teratogenicity) study.
GLP	Yes.
Year	1987.
Species	Rat.
Strain	CD (Sprague-Dawley).
Route of administration	Inhalation (gas).
Concentration levels	0, 40, 200, or 1000 ppm.
Sex	24-28 pregnant females per group.
Exposure period	Days 6-15 of gestation.
Frequency of treatment	6 hours/day.
Control group and treatment	Air-exposed only.
Duration of test	Females sacrificed on gestation day 20.
Statistical methods	Analysis of variance for body weights, number of resorptions, implants, live, dead or affected fetuses per litter. Significant differences among the groups were also analyzed by Duncan's multiple range test or arcsin transformation of the response proportion. Binary-response variables between groups were compared using chi-square or Fisher's exact test.
Remarks for Test Conditions.	Female rats were mated to unexposed males and exposed from days 6-15 of gestation to 0, 40, 200, or 1000 ppm of the test substance. Analytical chamber concentrations were measured by on-line gas chromatography. Body weights were recorded on gestation days 0, 6, 11, 16, and 20. Maternal animals were observed daily for mortality, morbidity, and signs of toxicity and examined for gross tissue abnormalities at necropsy (day 20). The uterus and placenta was removed and weighed; the number of implantation sites, resorptions, live and dead fetuses were recorded. Live fetuses were weighed and subjected to external, visceral, and skeletal examinations. Approximately 50% of the fetal heads were sectioned and examined.
Results	
NOAEL maternal toxicity	200 ppm
NOAEL developmental	1000 ppm
toxicity	The only toxicity 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 significant 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.
Conclusions	

(study author)	There was no evidence of teratagenicity or adverse reproductive effects in any of the exposed groups.
Data Quality	
Reliabilities	Reliable without restrictions. Guideline study.
References	Morrissey, R.E., Schwetz, B.A., Hackett, P.L., Sikov, M.R., Hardin, B.D., McClanahan, B.J., Decker, J.R., and Mast, T.J. (1990). Overview of Reproductive and Developmental Toxicity Studies of 1,3-Butadiene in Rodents. Environ. Health Perspect. 86:79-84.
Other	Robust Summary Prepared by ExxonMobil Biomedical Sciences, Inc.
Las*t changed*	20-Oct-99

Toxicity to Reproduction

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity 99.88%
Method	
Method/guideline followed	Other.
Test type	Sperm-head morphology assay.
GLP	Yes.
Year	1987.
Species	Mouse.
Strain	B6C3F1.
Route of administration	Inhalation (gas).
Concentration levels	0, 200, 1000, and 5000 ppm.
Sex	20 males per group.
Exposure period	6 hours/day.
Frequency of treatment	5 days.
Control group and treatment	Air-exposed only.
Duration of test	Males sacrificed 5 weeks post-exposure.
Statistical methods	Normal and abnormal sperm heads were expressed as percentage of the total number of cells examined. These data were subjected to arcsin transformation and evaluated by analysis of variance. If significant, Duncan's multiple range test was used for intergroup differences. Dose response trends were determined by orthogonal contrast.
Remarks for Test Conditions.	The mice were observed twice daily and body weights recorded weekly. During the fifth week post-exposure the mice were sacrificed and examined for lesions of the reproductive tract and other gross abnormalities. Sperm was obtained from the cauda of the right epididymis. Slides were prepared, stained, and examined microscopically. The morphology of at least 500 sperm heads per mouse was categorized.
Results	
NOAEL	200 ppm The percentage of abnormal sperm heads increased with exposure concentration: 1.61% (0 ppm), 1.95% (200 ppm), 2.79% (1000 ppm), and 3.79% (5000 ppm). Only the values for the 1000 and 5000 ppm groups were significantly different from the control ($p < 0.05$). Only a single timepoint was examined, so the effect on all stages of spermatogenesis could not be determined.
Conclusions	
(Study author)	These results suggest that the test substance affected spermatogenesis in mice at 1000 and 5000 ppm, but the effect of this observation on other reproductive endpoints is not known.
Data Quality	
Reliabilities	Reliable with restrictions. Acceptable, well-documented publication which meets basic scientific principles.
References	Morrissey, R.E., Schwetz, B.A., Hackett, P.L., Sikov, M.R.,

	Hardin, B.D., McClanahan, B.J., Decker, J.R., and Mast, T.J. (1990). Overview of Reproductive and Developmental Toxicity Studies of 1,3-Butadiene in Rodents. Environ. Health Perspect. 86:79-84.
Other	Robust Summaries Prepared by ExxonMobil Biomedical Sciences, Inc.
Las*t changed*	20-Oct-99

Toxicity to Reproduction

Test Substance	
Remarks	1,3-butadiene, CAS# 106-99-0 Purity 99.88%
Method	
Method/guideline followed	Other.
Test type	Rodent dominant lethal test.
GLP	Yes.
Year	1987.
Species	Mouse
Strain	CD-1 (Swiss).
Route of administration	Inhalation (gas).
Concentration levels	0, 200, 1000, and 5000 ppm.
Sex	20 males per group.
Exposure period	6 hours/day.
Frequency of treatment	5 days.
Control group and treatment	Air-exposed only.
Duration of test	8 weeks post-exposure.
Statistical methods	The number of implantation sites and intrauterine deaths per litter for each week were analyzed by analysis of variance. When appropriate, proportions of resorptions and dead or live fetuses per implant were subjected to arcsin transformation and evaluated by analysis of variance. If significant, Duncan's multiple range test was used for intergroup differences.
Remarks for Test Conditions.	After five days of exposure, the male mice were mated with unexposed females (two females per week for each male for 8 consecutive weeks). Females were removed from cohabitation after 7 days sacrificed 12 days later and the uterine contents examined. Observations included: the total number, position, and status of implantations; the numbers of early and late resorptions; and numbers of live and dead fetuses.
Results	Slight statistically significant effects were noted in the mated females for three endpoints during the first 2 weeks post-exposure: ratio of dead to total implants, percentage of females with $\geq$2 dead implants, and number of dead implants per pregnancy. However, these observations only occurred in the two lower exposure groups (except for increased number dead implants/pregnancy in the 5000 ppm group during week 1). There were no differences for number of pregnant females, implantations per litter, number of live fetuses, dead implantations per total implantations, or number of resorptions during weeks 1 and 2. There were no differences for any endpoint during weeks 3-8.
Conclusions	
(Study author)	The authors concluded that the results observed during the first two weeks are consistent with an adverse effect on more mature germ cells (spermatozoa and spermatids) however considering the lack of effects in the high exposure group the findings are not clear for a

	dose-dependent response.
Data Quality	
Reliabilities	Reliable with restrictions. Acceptable, well-documented publication which meets basic scientific principles.
References	Morrissey, R.E., Schwetz, B.A., Hackett, P.L., Sikov, M.R., Hardin, B.D., McClanahan, B.J., Decker, J.R., and Mast, T.J. (1990). Overview of Reproductive and Developmental Toxicity Studies of 1,3-Butadiene in Rodents. Environ. Health Perspect. 86:79-84.
Other	Robust Summary Prepared by Exxon Biomedical Sciences, Inc.
Las*t changed*	20-Oct-99

Genetic Toxicity - *in vivo*

Test Substance	
Remarks	C4 Crude Butadiene (Low 1,3-Butadiene Content) approx. composition: 10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% trans-2-butene, 29% 1-butene, 11% isobutylene, 12% cis-2-butene Primary CAS #: 68476-52-8 Other CAS #s in the stream: 25167-67-3, 64742-83-2, 68187-60-0, 68476-44-8, 68955-28-2, and 68956-54-7.
Method	
Method/guideline followed	U.S. EPA OPPTS 870.5395 (1998) and OECD # 474 (1997) guidelines.
Type	Mammalian erythrocyte micronucleus assay.
GLP	Yes.
Year	2001.
Species	Mouse.
Strain	B6C3F1
Sex	Male and Female
Route of administration	Inhalation (gas).
Doses/concentration levels	0, 0.5, 10.0, or 20.0 mg/L.
Exposure period	4 hours/day for 2 days.
Statistical methods	The raw data on the counts of MN-PCE for each animal were first transformed by adding one (1) to each count and then taking the natural log of the adjusted number. The transformed MN-PCE data and the data on percent PCE were analyzed separately by a two-way analysis of variance (Winer, 1971). The sex-by-dose interaction in the two-way analysis was reviewed and if significant, a one-way analysis was performed for each sex. Pairwise comparisons of treated vs. control groups were done, if the dose effect was significant, by Dunnett's t-test, one-sided (upper) for MNPCE and two-sided for the percent PCE (Winer 1971). Linear dose-related trend tests were performed only if any of the pairwise comparisons yielded significant differences. The alpha level at which all tests were conducted was 0.05.
Remarks for Test Conditions.	Groups of six male B6C3F1 mice (approximately 26g, 9 weeks old) and six female B6C3F1 mice (approximately 21g, 9 weeks old) were exposed whole-body inhalation to target concentrations of 0, 0.5, 10.0, and 20.0 mg/L of the C4 Crude Butadiene, Low 1,3-Butadiene Content. All inhalation exposures occurred under dynamic airflow conditions and chamber concentrations were monitored by analytical methods. Inhalation exposures occurred on two consecutive days, 4 hours per day. A positive control group was dosed by oral gavage with 120 mg/kg of cyclophosphamide approximately 24 hours before sacrifice. Groups of animals (6/sex/dose) were sacrificed at 24 hours after the second treatment for the collection of femoral bone marrow to evaluate the incidence of micronuclei (MN) in polychromatic erythrocytes (2000 PCE/animal) The proportion of PCE among erythrocytes in the bone marrow was estimated by examining 200

	erythrocytes/animal.
Results	Statistically significant increases in the frequencies of MN-PCE in both sexes of all groups treated with the test material were observed as compared to the negative controls. Although statistical analyses indicated a significant dose response, the difference in MN-PCE incidence at the high- (20 mg/L) and low- (0.5 mg/L) dose was minimal. The positive control treatment induced a significant increase in the frequency of MN-PCE. The mean proportion of PCE among the erythrocytes (200/animal) in the bone marrow was not affected following exposure to the test material while the positive control treatment significantly reduced this value.
Conclusions	
(study author)	C4 Crude Butadiene (low 1,3-butadiene content) was positive for the induction of micronuclei in this test system under the experimental conditions used.
Data Quality	
Reliabilities	Reliable without restrictions.
References	Organisation for Economic Co-Operation and Development (OECD) (1997). Guidelines for Testing of Chemicals. #474. Genetic Toxicology: Micronucleus Test, OECD Publication Service, 2 Rue Andre-Pascal, 75775 Paris Cedex 16, France. U.S. EPA (1998). Office of Prevention, Pesticides and Toxic Substances, OPPTS 870.5395. *In Vivo Mammalian Bone Marrow Cytogenetic Tests - Micronucleus assay* Winer, B. J. (1971). *Statistical Principles in Experimental Design* (2nd Edition). McGraw-Hill, New York, New York. Spencer, T.J., Hammond, T.A., Houtman, C.E. and Marty, G.T. (2001). The valuation of C4 crude butadiene (low 1,3-butadiene content) in the mouse bone marrow micronucleus test by an inhalation exposure - multiple exposures followed by a single sampling point. Report of The Dow Chemical Company conducted for the American Chemistry Council, Olefins Panel.
Other	Last updated: Robust summary prepared by contractor to Olefins Panel

Repeated Dose Toxicity

Test Substance	
Remarks	C4 Crude Butadiene (low 1,3-Butadiene Content), approx. composition: 10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% trans-2-butene, 29% 1-butene, 11% isobutylene, 12% cis-2-butene Primary CAS#: 68476-52-8; Other CAS #s used to represent this stream : 25167-67-3, 64742-83-2, 68187-60-0, 68476-44-8, 68955-28-2, and 68956-54-7
Method	
Method/guideline followed	OECD 422
Test type	Combined repeated exposure inhalation toxicity study with the reproduction / developmental screening test
GLP	Yes
Year	2001
Species	Rat
Strain	Crl:CD® (Sprague-Dawley) IGS BR
Route of administration	Inhalation (vapor).
Duration of test	36-37 days
Doses/concentration levels	0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3)
Sex	12 male, 12 female per group.
Exposure period	6 hours/day.
Frequency of treatment	7 days/week
Control group and treatment	12 male, 12 female, air-only exposed.
Post exposure observation period	Not applicable.
Statistical methods	Adult body weights, body weight gains, feed consumption, organ weights, clinical chemistry data and appropriate hematologic data were evaluated by ANOVA. Detailed clinical observation incidence scores for ranked observations and sensory evaluation scores were statistically analyzed by a z-test of proportions. Rectal temperature and grip performance were analyzed by an analysis of covariance with dose as the factor and time as the covariate. Motor activity was analyzed by a repeated-measure design with treatment as a between-subjects factor and the repeated factor of time.
Test Conditions	Groups of 12 male and 12 female CD rats were exposed to vapors of the test material daily by inhalation for approximately six hours/day at exposure levels of 0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3). The main study (repeated-exposure general toxicity and neurotoxicity endpoints) males and females were exposed for 36 and 37 days, respectively. Effects on general toxicity, neurobehavioral activity, clinical chemistry, and hematology were evaluated. In addition, a gross necropsy with extensive histopathologic examination of tissues was conducted. The study also contained reproductive and developmental toxicity satellite groups (summarized separately).

Results	
NOAEL (NOEL)	20 mg/L (20,000 mg/mg^3).
LOAEL (LOEL)	Not applicable.
Remarks	Actual time-weighted averages for total olefins for the 2, 10 and 20 mg/L (2,000; 10,000; or 20,000 mg/m^3) exposure groups were **2.17** ± 0.461, **9.81** ± 1.66, **19.1** ± 2.63 mg/L, respectively, over the 37 exposure days in the study. Owing in part to the nature of the test material, there were technical difficulties in generating vapors from the test material, such that targeted exposure concentrations were not met on one entire day and for brief periods on a few other days. However, the affected instances were limited relative to the total duration of the study and were considered to have no significant impact on study integrity. There were no deaths or treatment-related clinical observations noted. No significant differences in body weights or feed consumption were observed for the males or females at any dose level tested throughout the duration of the study. Sensory evaluation, rectal temperature, and fore/hindlimb grip performance data revealed no treatment-related findings. Treatment did not affect motor activity total counts (treatment-by-time interaction, p = 0.0930). However, the treatment-by-time-by-epoch interaction was significant (p = 0.0098). Examination of the data suggested that this effect could be reasonably attributed to the significant time-by-epoch interaction (p = 0.0001) rather than to a true treatment effect. This was confirmed following calculation of linear contrasts to determine which group(s), if any, were different from the control group. These analyses revealed that none of the three treatment groups were significantly different from control (alpha > 0.02) when the time-by-epoch-by-treatment interaction was considered. There were no treatment-related changes for males and females at any dose level for prothrombin time, hematology values or clinical chemistry measures. Females exposed to 2 mg/L had a statistically identified increase in hematocrit value, and a statistically identified decrease in serum total protein. Given the lack of dose response, effects on related parameters, and similar effects in males, these were considered incidental findings that were toxicologically insignificant. There were no effects of exposure on organ weights, gross pathology or histopathology in any of the treated groups when compared to their respective controls.
Conclusions	Repeated inhalation exposure of C4 Crude Butadiene, Low 1,3-Butadiene to male and female Sprague Dawley rats at levels of 0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3) produced no evidence of any adverse effects on clinical observations, organ weights, gross or histopathology, neurobehavioral activity, clinical chemistry or hematology endpoints. Based on these data, the no-observable-effect level

	(NOEL) for repeated dose toxicity was 20 mg/L, the highest concentration tested.
Data Quality	
Reliabilities	Klimisch value = 1 (Reliable without restrictions).
References	Carney, E.W., Liberacki, A.B., Thomas, J., Houtman, C.E. and Marable, B.R. (2001). C4 Crude butadiene, low 1,3-butadiene content: a combined repeated exposure inhalation toxicity study with the reproduction/developmental screening test in Sprague Dawley rats. Report of The Dow Chemical Company conducted for the American Chemistry Council, Olefins Panel.
Other	
Last changed	6-Aug-01 Robust summary prepared by contract to Olefins Panel

Toxicity to Reproduction

Test Substance	
Remarks	C4 Crude Butadiene (low 1,3-Butadiene Content) approx. composition: 10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% trans-2-butene, 29% 1-butene, 11% isobutylene, 12% cis-2-butene Primary CAS#: 68476-52-8; Other CAS #s used to represent this stream: 25167-67-3, 64742-83-2, 68187-60-0, 68476-44-8, 68955-28-2, and 68956-54-7
Method	
Method/guideline followed	OECD 422
Test type	Combined repeated exposure inhalation toxicity study with the reproduction / developmental screening test
GLP	Yes.
Year	2001
Species	Rat
Strain	Crl:CD® (Sprague-Dawley) IGS BR
Route of administration	Inhalation (vapor).
Duration of test	Two weeks prior to breeding, during breeding (up to two weeks), and continuing through day 19 of gestation. The dams were then allowed to deliver their litters, which were retained until postnatal day 4. The males were exposed for 36-37 days.
Doses/concentration levels	0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3)
Sex	12 male, 12 female per group.
Exposure period	6 hours/day.
Frequency of treatment	7 days/week
Control group and treatment	12 male, 12 female, air-only exposed.
Post exposure observation period	Not applicable.
Statistical methods	Adult body weights and feed consumption, maternal body weight gains, and pup body weights were analyzed by ANOVA. Gestation length, average time to mating (precoital interval) and litter size were analyzed using a nonparametric ANOVA. Pregnancy rates and mating, conception, fertility and gestation indices were analyzed by the Fisher exact probability test. Evaluation of the neonatal sex ratio was performed by the binomial distribution test. Post-implantation loss, pup survival indices, and other incidence data among neonates were analyzed using the litter as the experimental unit by a censored Wilcoxon test.
Test Conditions	Groups of 12 male and 12 female Sprague Dawley rats were exposed to vapors of the test material daily by inhalation for approximately six hours/day at exposure levels of 0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3). The study design included a main study for repeated dose toxicity end points (summarized separately) and reproductive / developmental toxicity satellite groups of 12 females per exposure level. The reproductive and developmental toxicity satellite groups were

	exposed for two weeks prior to breeding, during breeding (up to two weeks), and continuing through day 19 of gestation. Males from the main study were used to breed these females. The dams were allowed to deliver their litters, which were retained until postnatal day 4. Effects on general toxicity, gonadal function, mating behavior, implantation, and general fertility were evaluated in the satellite group adults, followed by a gross necropsy of the satellite group females on lactation day 5. Litter size, pup survival, sex, body weight, and the presence of gross external malformations was assessed in the offspring. The males were exposed for a total of 36 to 37 days, and were then necropsied. In addition to the repeated dose toxicity end points assessed (discussed separately), reproductive assessment of the males included mating, conception and fertility indices, reproductive organ weights and gross/histopathology of the reproductive tract. Testis histopathology included a qualitative assessment of stages of the spermatogenic cycle.
Results	
NOAEL (NOEL)	20 mg/L (20,000 mg/mg^3).
LOAEL (LOEL)	Not applicable.
Remarks	Actual time-weighted averages for total olefins for the 2, 10 and 20 mg/L (2,000; 10,000; or 20,000 mg/m^3) exposure groups were **2.17** ± 0.461, **9.81** ± 1.66, **19.1** ± 2.63 mg/L, respectively, over the 37 exposure days in the study. Owing in part to the nature of the test material, there were technical difficulties in generating vapors from the test material, such that targeted exposure concentrations were not met on one entire day and for brief periods on a few other days. However, the affected instances were limited relative to the total duration of the study and were considered to have no significant impact on study integrity. There were no deaths or treatment-related clinical observations noted. No significant differences in parental body weights, body weight gains or feed consumption were observed at any dose level tested throughout the duration of the study. The only exception to this was a statistically identified increase in feed consumption noted for the 10 mg/L satellite females during the premating period (days 7-14). However, this increase was considered spurious, as feed consumption increases were not noted during subsequent gestation and lactation periods and similar changes in feed consumption were not observed at the highest exposure level of 20 mg/L. There were no treatment-related effects at any dose level on any of the reproductive parameters evaluated in this study. These included measures of reproductive performance (mating, conception and fertility, time to mating, gestation length, litter size), offspring survival (gestation and postnatal survival indices, percent pre- and post-implantation loss), pup body weight and pup sex ratio. The only statistically identified

	change in any of these parameters was an increase in post-implantation loss occurring only at the low-dose. This was considered a spurious finding, given the lack of a dose response. Of the 12 females mated in each group, the number of viable litters produced was 11, 11, 11, and 12 for the 0, 2, 10 and 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3) exposure level groups, respectively. External morphological alterations observed in the pups were limited to a hernia observed in a single pup from the high dose group. Given the low incidence of this finding, it was considered spurious and unrelated to exposure.
Conclusions	Repeated inhalation exposure of C4 Crude Butadiene, Low 1,3-Butadiene to male and female Sprague Dawley rats at levels of 0, 2, 10, or 20 mg/L (0; 2,000; 10,000; or 20,000 mg/m^3) produced no evidence of adverse effects on any measures of reproductive function. Based on these data, the no-observable-effect level (NOEL) for reproductive toxicity was 20 mg/L, the highest concentration tested.
Data Quality	
Reliabilities	Klimisch value = 1 (Reliable without restrictions).
References	Carney, E.W., Liberacki, A.B., Thomas, J., Houtman, C.E. and Marable, B.R. (2001). C4 Crude butadiene, low 1,3-butadiene content: a combined repeated exposure inhalation toxicity study with the reproduction/developmental screening test in Sprague Dawley rats. Report of The Dow Chemical Company conducted for the American Chemistry Council, Olefins Panel.
Other	
Last changed	6-Aug-01 Robust summary prepared by contractor to Olefins Panel

Developmental Toxicity/Teratogenicity

Test Substance	
Remarks	C4 Crude Butadiene (low 1,3-Butadiene Content), approx. composition: 10% 1,3-butadiene, 4% isobutane, 4% n-butane, 29% trans-2-butene, 29% 1-butene, 11% isobutylene, 12% cis-2-butene Primary CAS#: 68476-52-8; Other CAS #s used to represent this stream : 25167-67-3, 64742-83-2, 68187-60-0, 68476-44-8, 68955-28-2, and 68956-54-7
Method	
Method/guideline followed	OECD 422
Test type	Combined repeated exposure inhalation toxicity study with the reproduction / developmental screening test
GLP	Yes.
Year	2001
Species	Rat
Strain	Crl:CD® (Sprague-Dawley) IGS BR
Route of administration	Inhalation (vapor).
Duration of test	Two weeks prior to breeding, during breeding (up to two weeks), and continuing through day 19 of gestation. The dams were then allowed to deliver their litters, which were retained until postnatal day 4.
Doses/concentration levels	0, 2, 10, or 20 mg/L
Sex	12 male, 12 female per group.
Exposure period	6 hours/day.
Frequency of treatment	7 days/week
Control group and treatment	12 male, 12 female, air-only exposed.
Post exposure observation period	Not applicable.
Statistical methods	Adult body weights and feed consumption, maternal body weight gains, and pup body weights were analyzed by ANOVA. Gestation length, average time to mating (precoital interval) and litter size were analyzed using a nonparametric ANOVA. Pregnancy rates and mating, conception, fertility and gestation indices were analyzed by the Fisher exact probability test. Evaluation of the neonatal sex ratio was performed by the binomial distribution test. Post-implantation loss, pup survival indices, and other incidence data among neonates were analyzed using the litter as the experimental unit by a censored Wilcoxon test.
Test Conditions	Groups of 12 male and 12 female Sprague Dawley rats were exposed to vapors of the test material daily by inhalation for approximately six hours/day at exposure levels of 0, 2, 10, or 20 mg/L. The study design included a main study for repeated dose toxicity end points (summarized separately) and reproductive / developmental toxicity satellite groups of 12 females per exposure level. The reproductive and developmental toxicity satellite groups were exposed for two weeks prior to breeding,

	during breeding (up to two weeks), and continuing until day 19 of gestation. Males from the main study were used to breed these females. The dams were allowed to deliver their litters, which were retained until postnatal day 4. Effects on general toxicity, gonadal function, mating behavior, implantation, and general fertility were evaluated in the satellite group adults, followed by a gross necropsy of the satellite group females on lactation day 5. Litter size, pup survival, sex, body weight, and the presence of gross external malformations was assessed in the offspring.
Results	
NOAEL (NOEL)	20 mg/L.
LOAEL (LOEL)	Not applicable.
Remarks	Actual time-weighted averages for total olefins for the 2, 10 and 20 mg/L exposure groups were **2.17** ± 0.461, **9.81** ± 1.66, **19.1** ± 2.63 mg/L, respectively, over the 37 exposure days in the study. Owing in part to the nature of the test material, there were technical difficulties in generating vapors from the test material, such that targeted exposure concentrations were not met on one entire day and for brief periods on a few other days. However, the affected instances were limited relative to the total duration of the study and were considered to have no significant impact on study integrity. There were no deaths or treatment-related clinical observations noted. No significant 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 at any dose level on any of the reproductive parameters evaluated in this study. These included measures of reproductive performance (mating, conception and fertility , time to mating, gestation length, litter size), offspring survival (gestation and postnatal survival indices, percent pre- and post-implantation loss), pup body weight and pup sex ratio. The only statistically identified change in any of these parameters was an increase in post-implantation loss occurring only at the low-dose. This was considered a spurious finding, given the lack of a dose response. Of the 12 females mated in each group, the number of viable litters produced was 11, 11, 11, and 12 for the 0, 2, 10 and 20 mg/L exposure level groups, respectively. External morphological alterations observed in the pups were limited to a hernia observed in a single pup from the high dose group. Given the low incidence of this finding, it was considered to be a spontaneous finding unrelated to exposure.
Conclusions	Repeated inhalation exposure of C4 Crude Butadiene, Low 1,3-Butadiene to male and female Sprague Dawley rats at levels of 0, 2, 10, or 20 mg/L produced no evidence of developmental toxicity or teratogenicity, as assessed in the OECD 422 study design. Based on these data, the no-observable-effect level (NOEL) for developmental toxicity was 20 mg/L, the highest

	concentration tested.
Data Quality	
Reliabilities	Klimisch value = 1 (Reliable without restrictions).
References	Carney, E.W., Liberacki, A.B., Thomas, J., Houtman, C.E. and Marable, B.R. (2001). C4 Crude butadiene, low 1,3-butadiene content: a combined repeated exposure inhalation toxicity study with the reproduction/developmental screening test in Sprague Dawley rats. Report of The Dow Chemical Company conducted for the American Chemistry Council Olefins Panel.
Other	
Last changed	6-Aug-01 Robust summary prepared by contractor to Olefins Panel

AQUATIC TOXICITY ROBUST SUMMARIES

Fish Acute Toxicity

Test Substance*:	Other TS
Method/Guideline*:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type):	Acute Fish Toxicity Calculation; LC50
GLP:	Not applicable
Year (study performed):	Not applicable
Species:	Freshwater Fish (calculated toxicity values are not species specific)
Analytical Monitoring:	Not applicable
Exposure Period:	96 hours
Statistical Method: (FT - ME)*	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPIWIN computer model (2). KOWWIN also has a database of experimental Kow values (EXPKOW.DB). The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of toxicity data for component chemicals is an estimate of the potential toxicity of category products. Chemical — Calculated log K_{ow} — Measured* log K_{ow} Isobutane — 2.23 — 2.76 n-butane — 2.31 — 2.89 isobutylene — 2.23 — 2.34 cis-butene-2 — 2.09 — 2.31 trans-butene-2 — 2.09 — 2.33 butene-1 — 2.17 — 2.40 1,3-butadiene — 2.03 — 1.99

	* Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the fish acute toxicity range of this category are C4 hydrocarbons that are common across the 10 CAS numbers (see Test Substance). Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (3). 1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92. 2. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. 3. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**	Calculated fish acute toxicity values for 7 chemicals representative of products in the Crude Butadiene C4 Category are as follows: Chemical — Calculated log K_{ow} — Fish Acute 96-hr LC50 (mg/L) Isobutane — 2.23 — 26.19 n-butane — 2.31 — 22.03 isobutylene — 2.23 — 25.28 cis-butene-2 — 2.09 — 34.23 trans-butene-2 — 2.09 — 34.23 butene-1 — 2.17 — 28.79 1,3-butadiene — 2.03 — 37.59

	Chemical / Measured* log K_{ow} / Fish Acute 96-hr LC50 (mg/L) Isobutane 2.76 8.32 n-butane 2.89 6.28 isobutylene 2.34 19.93 cis-butene-2 2.31 21.26 trans-butene-2 2.33 20.36 butene-1 2.40 17.50 1,3-butadiene 1.99 40.98 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated Kow values, products in this category are expected to have a fish 96-hour LC50 range of 22.03 to 37.59 mg/L. Based on the measured Kow values, products in this category are expected to have a fish 96-hour LC50 range of 6.28 to 40.98 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The toxicity values are calculated.
Reference: (FT - RE)	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for " acute toxicity to fish ". Selecting this option refers the reader to information in the "freetext" field for "test substance".

FT - Freetext
IUCLID fields include:
- RL - Reliability
- TC - Test Conditions
- RE - Reference
- RS - Results
- TS - Test Substance
- SO - Source
- CL - Conclusion

Daphnid Acute Toxicity

Test Substance*:	Other TS
Method/Guideline*:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type):	Acute Daphnid Toxicity Calculation; LC50
GLP:	Not applicable
Year (study performed):	Not applicable
Species:	Daphnid (calculated toxicity values are not species specific)
Analytical Monitoring:	Not applicable
Exposure Period:	48 hours
Statistical Method: (FT - ME)*	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPIWIN computer model (2). KOWWIN also has a database of experimental Kow values (EXPKOW.DB). The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of toxicity data for component chemicals is an estimate of the potential toxicity of category products. Chemical — Calculated log K_{ow} — Measured* log K_{ow} Isobutane — 2.23 — 2.76 n-butane — 2.31 — 2.89 isobutylene — 2.23 — 2.34 cis-butene-2 — 2.09 — 2.31 trans-butene-2 — 2.09 — 2.33 butene-1 — 2.17 — 2.40 1,3-butadiene — 2.03 — 1.99 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured

values.

Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4.

The seven chemicals selected to represent the daphnid acute toxicity range of this category are C4 hydrocarbons that are common across the 10 CAS numbers (see Test Substance). Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (3).

1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92.
2. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
3. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.

Results: (FT - RS)

Units/Value:

- **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**

Calculated daphnid acute toxicity values for 7 chemicals representative of products in the Crude Butadiene C4 Category are as follows:

Chemical	Calculated log K_{ow}	Daphnid Acute 48-hr LC50 (mg/L)
Isobutane	2.23	28.51
n-butane	2.31	24.11
isobutylene	2.23	27.53
cis-butene-2	2.09	36.91
trans-butene-2	2.09	36.91
butene-1	2.17	31.21
1,3-butadiene	2.03	40.27

Chemical	Measured* log K_{ow}	Daphnid Acute 48-hr LC50 (mg/L)

	Isobutane 2.76 9.39 n-butane 2.89 7.15 isobutylene 2.34 21.86 cis-butene-2 2.31 23.28 trans-butene-2 2.33 22.32 butene-1 2.40 19.28 1,3-butadiene 1.99 43.88 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated Kow values, products in this category are expected to have a daphnid 48-hour LC50 range of 24.11 to 40.27 mg/L. Based on the measured Kow values, products in this category are expected to have a daphnid 48-hour LC50 range of 7.15 to 43.88 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The toxicity values are calculated.
Reference: (FT - RE)	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for " acute toxicity to aquatic invertebrates ". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext
IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

Alga Toxicity

Test Substance*:	Other TS
Method/Guideline*:	Other: ECOSAR Computer Model
Year (guideline):	1999
Type (test type):	Green Alga Toxicity Calculation; EC50
GLP:	Not applicable
Year (study performed):	Not applicable
Species:	Freshwater Green Alga (calculated toxicity values are not species specific)
Analytical Monitoring:	Not applicable
Exposure Period:	96 hours
Statistical Method: (FT - ME)*	Not applicable
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, volume, replication, water quality parameters, environmental conditions, organisms supplier, age, size, weight, loading.**	Log Kow (octanol/water partition coefficient) values and a chemical structure are needed to calculate aquatic toxicity using the ECOSAR model. The Kow calculation is performed by KOWWIN based on an atom/fragment contribution method of Meylan and Howard (1), which is a subroutine in the EPIWIN computer model (2). KOWWIN also has a database of experimental Kow values (EXPKOW.DB). The following chemicals are representative of products in the Crude Butadiene C4 Category, which are complex, multi-constituent substances. The range of toxicity data for component chemicals is an estimate of the potential toxicity of category products. Chemical — Calculated log K_{ow} — Measured* log K_{ow} Isobutane — 2.23 — 2.76 n-butane — 2.31 — 2.89 isobutylene — 2.23 — 2.34 cis-butene-2 — 2.09 — 2.31 trans-butene-2 — 2.09 — 2.33 butene-1 — 2.17 — 2.40 1,3-butadiene — 2.03 — 1.99 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more

	than 13,000 organic compounds with reliably measured values.. Commercial products in this category can have a carbon number distribution predominantly between C3 and C5. These products can contain significant levels of 1,3-butadiene and similar low molecular weight olefins, which is why they are considered a category for purposes of the High Production Volume Chemical Program, and designated Crude Butadiene C4. The seven chemicals selected to represent the alga toxicity range of this category are C4 hydrocarbons that are common across the 10 CAS numbers (see Test Substance). Crude butadiene category products arise from production processes associated with ethylene manufacturing. More information on the Crude Butadiene C4 Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (3). 1. Meylan, W. and P. Howard. 1995. Atom/fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84:83-92. 2. Meylan, M., SRC 1994-1999. KOWWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. 3. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The Crude Butadiene C4 Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method, biological observations, control survival.**	Calculated alga toxicity values for 7 chemicals representative of products in the Crude Butadiene C4 Category are as follows: Chemical — Calculated log K_{ow} — Alga Toxicity 96-hr EC50 (mg/L) Isobutane — 2.23 — 18.06 n-butane — 2.31 — 15.35 isobutylene — 2.23 — 17.44 cis-butene-2 — 2.09 — 23.19 trans-butene-2 — 2.09 — 23.19 butene-1 — 2.17 — 19.71 1,3-butadiene — 2.03 — 25.27 Measured* — Alga Toxicity

	Chemical / log K_{ow} / 96-hr EC50 (mg/L) Isobutane 2.76 6.13 n-butane 2.89 4.71 isobutylene 2.34 13.94 cis-butene-2 2.31 14.81 trans-butene-2 2.33 14.22 butene-1 2.40 12.33 1,3-butadiene 1.99 27.42 * Experimental K_{ow} values supplied by the KOWWIN program database (EXPKOW.DB) which contains more than 13,000 organic compounds with reliably measured values.
Test Substance: (FT - TS)	25167-67-3 Butenes 68477-41-8 Distillate (Petroleum), Extractive C3-5 68955-28-2 Gases, (Petroleum) Light Steam Cracked, Butadiene Concentrate 68476-44-8 Hydrocarbons, >C3 68512-91-4 Hydrocarbons C3 – C4 Rich Petroleum Distillates 68187-60-0 Hydrocarbons, C4, Ethane-Propane Cracked 68476-52-8 Hydrocarbons, C4, Ethylene Manufactured By-Product 68956-54-7 Hydrocarbons C4, Unsaturated 69103-05-5 Hydrocarbons, C4-7, Butadiene Manufactured By-Product 64742-83-2 Naphtha, (Petroleum), Light Steam-Cracked
Conclusion: (FT - CL)	Based on the calculated Kow values, products in this category are expected to have an alga 96-hour EC50 range of 15.35 to 25.27 mg/L. Based on the measured Kow values, products in this category are expected to have an alga 96-hour EC50 range of 4.71 to 27.42 mg/L.
Reliability: (FT - RL)	(2) Reliable with restrictions The toxicity values are calculated.
Reference: (FT - RE)	Cash, G. and V. Nabholz. 1999. ECOSAR Classes for Microsoft Windows, ECOWIN v0.99e. U.S. Environmental Protection Agency, OPPT - Risk Assessment Division. Washington, DC, USA.
Other (source): (FT - SO)	American Chemistry Council, Olefins Panel

* Other TS is an option in the "test substance" pick list within the IUCLID data entry field for "acute toxicity to aquatic plants". Selecting this option refers the reader to information in the "freetext" field for "test substance".
FT - Freetext

IUCLID fields include:

RL - Reliability
TC - Test Conditions
RE - Reference
RS - Results
TS - Test Substance
SO - Source
CL - Conclusion

ROBUST SUMMARIES PART 2

HIGH BENZENE NAPHTHAS ROBUST SUMMARIES:

PHYSICAL-CHEMICAL PROPERTIES AND ENVIRONMENTAL FATE

ARE ALSO USED FOR PYROLYSIS C3+ AND C4+

HIGH BENZENE NAPHTHAS ROBUST SUMMARY

Boiling Point

Test Substance*:	Other TS [CAS # 64741-99-7; 64742-49-0; 64742-73-0; 64742-83-2; 64742-91-2; 67891-79-6; 67891-80-9; 68410-97-9; 68475-70-7; 68476-45-9; 68526-77-2; 68606-10-0; 68606-28-0; 68921-67-5; 68955-29-3; 68956-52-5; 68956-70-7; 69013-21-4; 8030-30-6]
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Pressure:	760 mm Hg
Test Conditions: • **Note: Concentration prep., vessel type, replication, test conditions.**	Boiling Point is calculated by the MPBPWIN subroutine, which is based on the calculation method of S. Stein and R. Brown in "Estimation of Normal Boiling Points from Group Contributions". 1994. J. Chem. Inf. Comput. Sci. 34: 581-587.
Results: **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Calculated and measured boiling point data for representative constituents of the High Benzene Naphthas Category are listed below. The data identify a potential boiling point range for substances represented by the 19 CAS numbers under Test Substance. Substances in this category do not have a specific boiling point value. Actual boiling point ranges for substances in this category will vary dependent on their constituent composition. Commercial substances in this category consist of both high purity hydrocarbons and complex hydrocarbon reaction products with a carbon number distribution that is predominantly C5-C11. The 12 chemicals selected to represent the boiling point range of this category are C5-C10 hydrocarbons that can be found in substances identified by the 19 CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, and olefinic process (distillation) knowledge.
Results: (continued) **Units/Value:** **Note: Deviations from protocol or guideline, analytical method.**	Substance Constituent / Calculated BP (°C) / Measured* BP (°C) Isoprene: 34.95 / 34.0 n-pentane: 46.01 / 36.0

	1,3-cyclopentadiene 69.17 41.0 Isohexane 56.26 63.2 n-hexane 71.53 68.7 methylcyclopentane 80.34 71.8 benzene 102.24 80.0 toluene 125.72 110.6 m-xylene 148.29 139.1 styrene 146.65 145.0 dicyclopentadiene 176.78 170.0 naphthalene 231.64 217.9 * Experimental values from EPIWIN database. The data represent a potential boiling point range for substances represented by the 19 CAS numbers under Test Substance.
Test Substance:	The High Benzene Naphthas Category includes the following CAS numbers: 64741-99-7 Extracts, petroleum, light naphtha solvent 64742-49-0 Naphtha, petroleum, hydrotreated light 64742-73-0 Naphtha, petroleum, hydrodesulfurized light 64742-83-2 Naphtha, petroleum, light steam-cracked 64742-91-2 Distillates, petroleum, steam-cracked 67891-79-6 Distillates, petroleum, heavy aromatic 67891-80-9 Distillates, petroleum, light aromatic 68410-97-9 Distillates, petroleum, light distillate hydrotreating process, low-boiling 68475-70-7 Aromatic hydrocarbons, C6-8, naphtha-raffinate pyrolyzate-derived 68476-45-9 Hydrocarbons, C5-10 aromatic concentration, ethylene-manufacture-by-product 68526-77-2 Aromatic hydrocarbons, ethane cracking scrubber effluent and flare drum 68606-10-0 Gasoline, pyrolysis, debutanizer bottoms 68606-28-0 Hydrocarbons, C5 and C10-aliphatic and C6-8-aromatic 68921-67-5 Hydrocarbons, ethylene-manufacture-by-product distillation residues 68955-29-3 Distillates, petroleum, light thermal cracked, debutanized aromatic 68956-52-5 Hydrocarbons, C4-8 68956-70-7 Petroleum products, C5-12, reclaimed, wastewater treatment 69013-21-4 Fuel oil, pyrolysis 8030-30-6 Naphtha High Benzene Naphthas Category substances arise from production processes associated with ethylene manufacturing. The 19 CAS numbers are used to describe the ten process streams arising from the ethylene process and other associated manufacturing processes. The category includes hydrocarbon product streams associated with the ethylene industry that contain significant levels of benzene, generally with a benzene content greater than 10% and averaging about 55%. More information on the High Benzene Naphthas Category can be

	found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The High Benzene Naphthas Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	The calculated boiling points for some representative constituents that are present in the category streams vary from 34.95 to 231.64°C @ 760 mm Hg. The measured boiling points of these same constituents vary from 34.0 to 217.9°C @ 760 mm Hg. Although this does not define the actual boiling points of the category streams, it offers an indication of a range that might be expected to encompass the boiling points of these complex streams with variable compositions. Boiling points outside of these ranges may be possible for some category streams.
Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by EPIWIN and measured data for specific chemicals as cited in the EPIWIN database. The data represent a potential boiling point range for substances represented by the 19 CAS numbers listed under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in High Benzene Naphthas Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for boiling point range based on constituent data.
Reference:	EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. (Boiling point values were calculated by the MPBPWIN subroutine and measured data came from the database in the computer program.)
Other (source):	American Chemistry Council, Olefins Panel (Prepared 7/03)

* Other TS is a selection option under the Test Substance pick list that is in the IUCLID entry field for Boiling Point. Selecting this option refers the reader to information in the test substance "freetext" field to which the CAS numbers can be added.

HIGH BENZENE NAPHTHAS ROBUST SUMMARY

Melting Point

Test Substance*:	Other TS [CAS # 64741-99-7; 64742-49-0; 64742-73-0; 64742-83-2; 64742-91-2; 67891-79-6; 67891-80-9; 68410-97-9; 68475-70-7; 68476-45-9; 68526-77-2; 68606-10-0; 68606-28-0; 68921-67-5; 68955-29-3; 68956-52-5; 68956-70-7; 69013-21-4; 8030-30-6]
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Test Conditions: • **Note: Concentration prep., vessel type, replication, test conditions.**	Melting Point is calculated by the MPBPWIN subroutine, which is based on the average result of the methods of K. Joback and Gold and Ogle. Joback's Method is described in Joback, K.G. 1982. A Unified Approach to Physical Property Estimation Using Multivariate Statistical Techniques. In The Properties of Gases and Liquids. Fourth Edition. 1987. R.C. Reid, J.M. Prausnitz and B.E. Poling, Eds. The Gold and Ogle Method simply uses the formula Tm = 0.5839Tb, where Tm is the melting point in Kelvin and Tb is the boiling point in Kelvin. The Gold and Ogle Method is described by Lyman, W.J., 1985, In: Environmental Exposure from Chemicals. Volume 1. Neely, W.B. and Blau, G.E. (eds), Boca Raton, FL, CRC Press, Inc., Chapter 2.
Results: **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Calculated and measured melting point data for representative constituents of the High Benzene Naphthas Category are listed below. The data identify a potential melting point range for substances represented by the 19 CAS numbers under Test Substance. Substances in this category do not have a specific melting point value. Actual melting point ranges for substances in this category will vary dependent on their constituent composition. Commercial substances in this category consist of both high purity hydrocarbons and complex hydrocarbon reaction products with a carbon number distribution that is predominantly C5-C11. The 12 chemicals selected to represent the melting point range of this category are C5-C10 hydrocarbons that can be found in substances identified by the 19 CAS numbers. Constituents representing category members were selected on the basis of
Results: (continued)	carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category

Units/Value: **Note: Deviations from protocol or guideline, analytical method.**	substances, and olefinic process (distillation) knowledge. Substance Constituent / Calculated MP (°C) / Measured* MP (°C) Isoprene -118.89 -145.9 n-pentane -106.92 -129.7 1,3-cyclopentadiene -91.83 -85.0 Isohexane -105.80 -162.9 n-hexane -93.84 -95.3 methylcyclopentane -85.82 -142.5 benzene -77.92 5.5 toluene -59.17 -94.9 m-xylene -40.69 -47.8 styrene -48.31 -31.0 dicyclopentadiene -16.78 32.0 naphthalene 5.01 80.2 * Experimental values from EPIWIN database. The data represent a potential melting point range for substances represented by the 19 CAS numbers under Test Substance.
Test Substance:	The High Benzene Naphthas Category includes the following CAS numbers: 64741-99-7 Extracts, petroleum, light naphtha solvent 64742-49-0 Naphtha, petroleum, hydrotreated light 64742-73-0 Naphtha, petroleum, hydrodesulfurized light 64742-83-2 Naphtha, petroleum, light steam-cracked 64742-91-2 Distillates, petroleum, steam-cracked 67891-79-6 Distillates, petroleum, heavy aromatic 67891-80-9 Distillates, petroleum, light aromatic 68410-97-9 Distillates, petroleum, light distillate hydrotreating process, low-boiling 68475-70-7 Aromatic hydrocarbons, C6-8, naphtha-raffinate pyrolyzate-derived 68476-45-9 Hydrocarbons, C5-10 aromatic concentration, ethylene-manufacture-by-product 68526-77-2 Aromatic hydrocarbons, ethane cracking scrubber effluent and flare drum 68606-10-0 Gasoline, pyrolysis, debutanizer bottoms 68606-28-0 Hydrocarbons, C5 and C10-aliphatic and C6-8-aromatic 68921-67-5 Hydrocarbons, ethylene-manufacture-by-product distillation residues 68955-29-3 Distillates, petroleum, light thermal cracked, debutanized aromatic 68956-52-5 Hydrocarbons, C4-8 68956-70-7 Petroleum products, C5-12, reclaimed, wastewater treatment 69013-21-4 Fuel oil, pyrolysis 8030-30-6 Naphtha
Test Substance: (continued)	High Benzene Naphthas Category substances arise from production processes associated with ethylene manufacturing. The 19 CAS numbers are used to describe the ten process streams arising from the ethylene process and other associated manufacturing processes. The category includes hydrocarbon

	product streams associated with the ethylene industry that contain significant levels of benzene, generally with a benzene content greater than 10% and averaging about 55%. More information on the High Benzene Naphthas Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The High Benzene Naphthas Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	The calculated melting points for some representative constituents that are present in the category streams vary from -118.89 to 5.01 °C. The measured melting points of these same constituents vary from -162.9 to 80.2°C. Although this does not define the actual melting points of the category streams, it offers an indication of a range that might be expected to encompass the melting points of these complex streams with variable compositions. Melting points outside of these ranges may be possible for some category streams.
Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by EPIWIN and measured data for specific chemicals as cited in the EPIWIN database. The data represent a potential melting point range for substances represented by the 19 CAS numbers listed under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the High Benzene Naphthas Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for melting point range based on constituent data.
Reference:	EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. (Melting point values were calculated by the MPBPWIN subroutine and measured data came from the database in the computer program.)
Other (source):	American Chemistry Council, Olefins Panel (Prepared 7/03)

* Other TS is a selection option under the Test Substance pick list that is in the IUCLID entry field for Melting Point. Selecting this option refers the reader to information in the test substance "freetext" field to which the CAS numbers can be added.

HIGH BENZENE NAPHTHAS ROBUST SUMMARY

Vapor Pressure

Test Substance*:	Other TS [CAS # 64741-99-7; 64742-49-0; 64742-73-0; 64742-83-2; 64742-91-2; 67891-79-6; 67891-80-9; 68410-97-9; 68475-70-7; 68476-45-9; 68526-77-2; 68606-10-0; 68606-28-0; 68921-67-5; 68955-29-3; 68956-52-5; 68956-70-7; 69013-21-4; 8030-30-6]
Method/Guideline:	Calculated values using MPBPWIN version 1.40, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: • **Note: Concentration prep., vessel type, replication, test conditions.**	Vapor Pressure is calculated by the MPBPWIN subroutine, which is based on the average result of the methods of Antoine and Grain. Both methods use boiling point for the calculation. The Antoine Method is described in the Handbook of Chemical Property Estimation. Chapter 14. W.J. Lyman, W.F. Reehl and D.H. Rosenblatt, Eds. Washington, D.C.: American Chemical Society. 1990. A modified Grain Method is described on page 31 of Neely and Blau's Environmental Exposure from Chemicals, Volume 1, CRC Press. 1985.
Results: **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Calculated and measured vapor pressure data for representative constituents of the High Benzene Naphthas Category are listed below. The data identify a potential vapor pressure range for substances represented by the 19 CAS numbers under Test Substance. Substances in this category do not have a specific vapor pressure value. Actual vapor pressure ranges for substances in this category will vary dependent on their constituent composition. Commercial substances in this category consist of both high purity hydrocarbons and complex hydrocarbon reaction products with a carbon number distribution that is predominantly C5-C11. The 12 chemicals selected to represent the vapor pressure range of this category are C5-C10 hydrocarbons that can be found in substances identified by the 19 CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, and olefinic process (distillation) knowledge.

	Substance Constituent / Calculated VP (hPa @ 25°C) / Measured* VP (hPa @ 25°C) Isoprene 7.35 E^2 7.33 E^2 n-pentane 6.84 E^2 6.85 E^2 1,3-cyclopentadiene 5.69 E^2 5.80 E^2 Isohexane 2.48 E^2 2.53 E^2 n-hexane 2.00 E^2 2.01 E^2 methylcyclopentane 1.77 E^2 1.84 E^2 benzene 1.16 E^2 1.26 E^2 toluene 31.60 37.86 m-xylene 8.83 11.05 styrene 6.73 8.53 dicyclopentadiene 2.20 3.05 naphthalene 0.05 0.11 * Experimental values from EPIWIN database. The data represent a potential vapor pressure range for substances represented by the 19 CAS numbers under Test Substance.
Test Substance:	The High Benzene Naphthas Category includes the following CAS numbers: 64741-99-7 Extracts, petroleum, light naphtha solvent 64742-49-0 Naphtha, petroleum, hydrotreated light 64742-73-0 Naphtha, petroleum, hydrodesulfurized light 64742-83-2 Naphtha, petroleum, light steam-cracked 64742-91-2 Distillates, petroleum, steam-cracked 67891-79-6 Distillates, petroleum, heavy aromatic 67891-80-9 Distillates, petroleum, light aromatic 68410-97-9 Distillates, petroleum, light distillate hydrotreating process, low-boiling 68475-70-7 Aromatic hydrocarbons, C6-8, naphtha-raffinate pyrolyzate-derived 68476-45-9 Hydrocarbons, C5-10 aromatic concentration, ethylene-manufacture-by-product 68526-77-2 Aromatic hydrocarbons, ethane cracking scrubber effluent and flare drum 68606-10-0 Gasoline, pyrolysis, debutanizer bottoms 68606-28-0 Hydrocarbons, C5 and C10-aliphatic and C6-8-aromatic 68921-67-5 Hydrocarbons, ethylene-manufacture-by-product distillation residues 68955-29-3 Distillates, petroleum, light thermal cracked, debutanized aromatic 68956-52-5 Hydrocarbons, C4-8 68956-70-7 Petroleum products, C5-12, reclaimed, wastewater treatment 69013-21-4 Fuel oil, pyrolysis 8030-30-6 Naphtha High Benzene Naphthas Category substances arise from production processes associated with ethylene manufacturing.

	The 19 CAS numbers are used to describe the ten process streams arising from the ethylene process and other associated manufacturing processes. The category includes hydrocarbon product streams associated with the ethylene industry that contain significant levels of benzene, generally with a benzene content greater than 10% and averaging about 55%. More information on the High Benzene Naphthas Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The High Benzene Naphthas Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	The calculated vapor pressures for some representative constituents that are present in the category streams vary from 0.05 to 7.35 E^2 hPa @ 25°C. The measured vapor pressures of these same constituents vary from 0.11 to 7.33 E^2 hPa @ 25°C. Although this does not define the actual vapor pressures of the category streams, it offers an indication of a range that might be expected to encompass the vapor pressures of these complex streams with variable compositions. Vapor pressure outside of these ranges may be possible for some category streams.
Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by EPIWIN and measured data for specific chemicals as cited in the EPIWIN database. The data represent a potential vapor pressure range for substances represented by the 19 CAS numbers under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the High Benzene Naphthas Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for vapor pressure range based on constituent data.
Reference:	EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. (Vapor pressure values were calculated by the MPBPWIN subroutine and measured data came from the database in the computer program.)
Other (source):	American Chemistry Council, Olefins Panel (Prepared 7/03)

* Other TS is a selection option under the Test Substance pick list that is in the IUCLID entry field for Vapor Pressure. Selecting this option refers the reader to information in the test substance "freetext" field to which the CAS numbers can be added.

HIGH BENZENE NAPHTHAS ROBUST SUMMARY

Water Solubility

Test Substance*:	Other TS [CAS # 64741-99-7; 64742-49-0; 64742-73-0; 64742-83-2; 64742-91-2; 67891-79-6; 67891-80-9; 68410-97-9; 68475-70-7; 68476-45-9; 68526-77-2; 68606-10-0; 68606-28-0; 68921-67-5; 68955-29-3; 68956-52-5; 68956-70-7; 69013-21-4; 8030-30-6]
Method/Guideline:	Calculated values using WSKOWWIN version 1.36, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: • **Note: Concentration prep., vessel type, replication, test conditions.**	Water Solubility is calculated by the WSKOWWIN subroutine, which is based on a Kow correlation method described by W. Meylan, P. Howard and R. Boethling in "Improved method for estimating water solubility from octanol/water partition coefficient". *Environ. Toxicol. Chem*. 15:100-106. 1995.
Results: **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Calculated and measured water solubility data for representative constituents of the High Benzene Naphthas Category are listed below. The data identify a potential water solubility range for substances represented by the 19 CAS numbers under Test Substance. Substances in this category do not have a specific water solubility value. Actual water solubility ranges for substances in this category will vary dependent on their loading rate (i.e., weight of test material added to a volume of water). Commercial substances in this category consist of both high purity hydrocarbons and complex hydrocarbon reaction products with a carbon number distribution that is predominantly C5-C11. The 12 chemicals selected to represent the water solubility range of this category are C5-C10 hydrocarbons that can be found in substances identified by the 19 CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, and olefinic process (distillation) knowledge.
Results: (continued) **Units/Value:** **Note: Deviations from protocol or**	Substance Constituent / Calculated WS (mg/L @ 25°C) / Measured WS* (mg/L @ 25°C) Isoprene — 247.2 — 338.6

guideline, analytical method.	n-pentane 159.70 49.8 1,3-cyclopentadiene 470.6 na Isohexane 66.94 31.1 n-hexane 57.42 17.2 methylcyclopentane 83.95 49.4 benzene 2634.0 2000.0 toluene 832.7 573.1 m-xylene 258.4 207.2 styrene 386.7 343.7 dicyclopentadiene 51.9 na naphthalene 183.8 142.1 * Experimental values from EPIWIN database. na = not available The data represent a potential water solubility range for substances represented by the 19 CAS numbers under Test Substance.
Test Substance:	The High Benzene Naphthas Category includes the following CAS numbers: 64741-99-7 Extracts, petroleum, light naphtha solvent 64742-49-0 Naphtha, petroleum, hydrotreated light 64742-73-0 Naphtha, petroleum, hydrodesulfurized light 64742-83-2 Naphtha, petroleum, light steam-cracked 64742-91-2 Distillates, petroleum, steam-cracked 67891-79-6 Distillates, petroleum, heavy aromatic 67891-80-9 Distillates, petroleum, light aromatic 68410-97-9 Distillates, petroleum, light distillate hydrotreating process, low-boiling 68475-70-7 Aromatic hydrocarbons, C6-8, naphtha-raffinate pyrolyzate-derived 68476-45-9 Hydrocarbons, C5-10 aromatic concentration, ethylene-manufacture-by-product 68526-77-2 Aromatic hydrocarbons, ethane cracking scrubber effluent and flare drum 68606-10-0 Gasoline, pyrolysis, debutanizer bottoms 68606-28-0 Hydrocarbons, C5 and C10-aliphatic and C6-8-aromatic 68921-67-5 Hydrocarbons, ethylene-manufacture-by-product distillation residues 68955-29-3 Distillates, petroleum, light thermal cracked, debutanized aromatic 68956-52-5 Hydrocarbons, C4-8 68956-70-7 Petroleum products, C5-12, reclaimed, wastewater treatment 69013-21-4 Fuel oil, pyrolysis 8030-30-6 Naphtha
Test Substance: (cont'd)	High Benzene Naphthas Category substances arise from production processes associated with ethylene manufacturing. The 19 CAS numbers are used to describe the ten process streams arising from the ethylene process and other associated manufacturing processes. The category includes hydrocarbon product streams associated with the ethylene industry that contain significant levels of benzene, generally with a benzene content greater than 10% and averaging about 55%.

	More information on the High Benzene Naphthas Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The High Benzene Naphthas Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	The calculated water solubility for some representative constituents that are present in the category streams vary from 51.9 to 2634.0 mg/L @ 25°C. The measured water solubility of these same constituents vary from 17.2 to 2000.0 mg/L @ 25°C. Although this does not define the actual water solubility of the category streams, it offers an indication of a range that might be expected to encompass the water solubility of these complex streams with variable compositions. Water solubilities outside of these ranges may be possible for some category streams.
Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by EPIWIN and measured data for specific chemicals as cited in the EPIWIN database. The data represent a potential water solubility range for substances represented by the 19 CAS numbers under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the High Benzene Naphthas Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for water solubility range based on constituent data.
Reference:	EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. (Water solubility values were calculated by the WSKOWWIN subroutine and measured data came from the database in the computer program.)
Other (source):	American Chemistry Council, Olefins Panel (Prepared 7/03)

* Other TS is a selection option under the Test Substance pick list that is in the IUCLID entry field for Water Solubility. Selecting this option refers the reader to information in the test substance "freetext" field to which the CAS numbers can be added.

HIGH BENZENE NAPHTHAS ROBUST SUMMARY

Hydrolysis (Stability in Water)

Test Substance*:	Other TS [CAS # 64741-99-7; 64742-49-0; 64742-73-0; 64742-83-2; 64742-91-2; 67891-79-6; 67891-80-9; 68410-97-9; 68475-70-7; 68476-45-9; 68526-77-2; 68606-10-0; 68606-28-0; 68921-67-5; 68955-29-3; 68956-52-5; 68956-70-7; 69013-21-4; 8030-30-6]
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
Type (test type):	Not applicable
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Analytical Monitoring:	Not applicable
Test Conditions: • **Note: Concentration preparation, vessel type, volume, replication, deviations from guideline or protocol**	Not applicable
Results: **Units/Value:** • **Note: Analytical method, observations, half-lives by pH, degradation products**	Not applicable
Test Substance:	The High Benzene Naphthas Category includes the following CAS numbers: 64741-99-7 Extracts, petroleum, light naphtha solvent 64742-49-0 Naphtha, petroleum, hydrotreated light 64742-73-0 Naphtha, petroleum, hydrodesulfurized light 64742-83-2 Naphtha, petroleum, light steam-cracked 64742-91-2 Distillates, petroleum, steam-cracked 67891-79-6 Distillates, petroleum, heavy aromatic 67891-80-9 Distillates, petroleum, light aromatic 68410-97-9 Distillates, petroleum, light distillate hydrotreating process, low-boiling 68475-70-7 Aromatic hydrocarbons, C6-8, naphtha-raffinate pyrolyzate-derived 68476-45-9 Hydrocarbons, C5-10 aromatic concentration, ethylene-manufacture-by-product

	68526-77-2 Aromatic hydrocarbons, ethane cracking scrubber effluent and flare drum 68606-10-0 Gasoline, pyrolysis, debutanizer bottoms 68606-28-0 Hydrocarbons, C5 and C10-aliphatic and C6-8-aromatic 68921-67-5 Hydrocarbons, ethylene-manufacture-by-product distillation residues 68955-29-3 Distillates, petroleum, light thermal cracked, debutanized aromatic 68956-52-5 Hydrocarbons, C4-8 68956-70-7 Petroleum products, C5-12, reclaimed, wastewater treatment 69013-21-4 Fuel oil, pyrolysis 8030-30-6 Naphtha High Benzene Naphthas Category substances arise from production processes associated with ethylene manufacturing. The 19 CAS numbers are used to describe the ten process streams arising from the ethylene process and other associated manufacturing processes. The category includes hydrocarbon product streams associated with the ethylene industry that contain significant levels of benzene, generally with a benzene content greater than 10% and averaging about 55%. More information on the High Benzene Naphthas Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The High Benzene Naphthas Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	**Summary** In the environment, hydrolysis will not contribute to the degradation of chemicals in the High Benzene Naphthas Category. The High Benzene Naphthas Category includes ten process streams: • **Pyrolysis Gasoline** • **Pyrolysis C6 Fraction** • **Pyrolysis C6-C8 Fraction** • **Pyrolysis C5-C6 Fraction** • **Hydrotreated C6 Fraction** • **Hydrotreated C6-C7 Fraction** • **Hydrotreated C6-C8 Fraction** • **Quench Loop Pyrolysis Oil and Compressor Oil** • **Recovered Oil from Waste Water Treatment** • **Extract from Benzene Extraction** Nineteen CAS numbers (see Test Substance) identify substances derived from these process streams. As discussed below, the chemicals in these streams are composed of carbon and hydrogen and are not amenable to hydrolysis because of their molecular structure and the chemical reaction required for this type of transformation to occur.

	The High Benzene Naphthas Category A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. The category includes hydrocarbon product streams associated with the ethylene industry that contain significant levels of benzene, generally with a benzene content greater than 10% and averaging about 55%. In some cases, petroleum refinery streams may be combined with intermediate streams from the ethylene unit and co-processed to produce these products. This grouping of CAS numbers represents hydrocarbon streams with a carbon number distribution that is predominantly C5-C11, through components boiling at 650°F or higher. That is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated High Benzene Naphthas. The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process). More information on the High Benzene Naphthas Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the ten process streams in this category are: • **Pyrolysis Gasoline** (Pygas) consists predominantly of C5+ hydrocarbons produced by the ethylene cracking furnaces. Typically the stream is derived from (1) the bottoms product from the debutanizer, (2) oils separated from furnace effluent quench systems, and (3) “drips” or condensate resulting from compression of the cracked gas. The oils from the quench systems and the “drips” may be stabilized to remove lights before blending with Pygas from the other sources. Depending on the plant configuration, Pygas may contain all of these intermediate streams, or the quench oils and stabilized drips may be transferred as separate streams. Low concentrations (e.g. 3% total) of C4 and lighter hydrocarbons may be present in the stream. A detailed analysis of Pygas may identify 60 or more hydrocarbon components or component groups, primarily unsaturated hydrocarbons and aromatics. Benzene, toluene, and dicyclopentadiene together may account for more than 50% of a Pygas stream and typically no other single component is present at a level greater than about 5%. The benzene concentration of Pygas is typically about 40% and the reported values range from 15 to 62%. The concentrations of individual hydrocarbon components in Pygas vary depending on the type of feedstock used by the ethylene plant, the mode of operation of the cracking furnaces (i.e. severity) and the ethylene process configuration. One non-typical Pygas stream is reported to contain vinylacetate at a concentration of up to about 10%. Vinylacetate is not typically found in ethylene process streams.

	• **Pyrolysis Gasoline Fractions (C5-C6, C6, and C6-C8 Fractions)** are separated by distillation into various boiling-point range fractions as intermediates in preparation for further processing. In some cases, petroleum refinery streams such as a C6 reformate fraction are combined with the pyrolysis gasoline prior to this separation. Similar to the situation for Pygas, the composition of these fractions vary depending on the ethylene process feedstock and the other operating variables. **1. Pyrolysis C5-C6 Fraction** has a carbon number distribution that is predominantly C5 to C6. One typical composition for this stream is reported as 70% benzene and 10% pentenes. **2. Pyrolysis C6 Fraction** has a carbon number distribution that is predominantly C6. Reported compositions vary from 35 to 77% benzene, 0.5 to 5% toluene with the balance primarily C6 non-aromatics, which are expected to be largely unsaturates. **3. Pyrolysis C6-C8 Fraction** has a carbon number distribution that is predominantly C6 to C8. The reported compositions range from 30 to 80% benzene, 15 to 25% toluene and 3 to 23% C8 aromatics. • **Hydrotreated Pyrolysis Fractions (C6, C6-C7, and C6-C8 Fractions)** are Pyrolysis gasoline or distillate fractions of pyrolysis gasoline that are treated with hydrogen over catalyst to saturate or partially saturate diolefins and/or olefins. In some cases, petroleum refinery streams such as a C6 reformate fraction are combined with the pyrolysis gasoline prior to this step. The hydrogenation process may be either one-stage or two-stage. The one-stage process is typically a liquid-phase process where the primary objective is to selectively convert diolefins to mono-olefins and to convert vinyl aromatics, for example, styrene to ethylbenzene. The second stage in a two-stage hydrogenation process is typically a vapor-phase, more severe hydrogenation that converts essentially all of the contained olefins to saturated hydrocarbons. A pygas fraction that will be processed by extraction or extractive distillation to produce high purity aromatics (benzene, toluene, or xylenes) is subjected to two-stage hydrogenation. Pygas fractions may be forwarded to hydrodealkylation units (less common) for benzene production after one-stage of hydrogenation. Hydrotreated Pyrolysis fractions may be the result of either one- or two-stage hydrogenation. 1. **Hydrotreated C6 Fraction** is very similar to the Pyrolysis C6 fraction except that the non-aromatics present in the hydrotreated stream are essentially all saturates. The reported composition for the Hydrotreated C6 stream indicates typical benzene content of 75%. 2. **Hydrotreated C6-C7 Fraction** has a carbon number distribution that is predominantly C6-C7 and the reported values indicate 40 to 70% benzene, and 3 to 15% toluene. 3. **Hydrotreated C6-C8 Fraction** has a reported typical composition of 40 to 60% benzene, 10 to 25% toluene, and 3 to 10% C8

	aromatics. • **Quench Loop Pyrolysis Oil and Compressor Oil** (Pyoil) represents higher boiling hydrocarbons that condense in the water quench system of an ethylene plant, typically at an ethylene unit cracking ethane, propane or butane. The stream can also include liquids collected at the cracked gas compressor knock out drums, which may include compressor injection oil. The carbon number distribution for Pyoil is C4 (or even lower) through heavier hydrocarbons such as naphthalene or even heavier. The reported typical composition includes 10 to 22% benzene and 5 to 11% toluene. • **Recovered Oil from Wastewater Treatment** can be expected to be of variable composition and made up largely of the components found in Pygas. No composition data or process specific information has been reported. Typically, water streams at ethylene units are processed to separate hydrocarbons from the water so that the water can be reused to generate steam for process-contact use (dilution steam for the cracking furnaces) or so that excess water can be forwarded to treatment prior to discharge or reuse. Water processing typically includes mechanical and gravity separation and steam or gas stripping. Hydrocarbons separated from the water in these systems are not usually isolated from the process. However, at least in one case, the Recovered Oil from Wastewater Treatment has been reported as an isolated intermediate. • **Extract from Benzene Extraction** are hydrotreated pyrolysis fractions containing aromatics (most commonly benzene or benzene and toluene) which are typically charged to extraction or extractive distillation units where the mixed aromatics are recovered. The carbon number distribution for this stream is predominantly C6 to C8. A reported typical concentration indicates 60 to 75% benzene, 25 to 40% toluene and 0 to 1% xylenes. **<u>Hydrolysis of Hydrocarbons as a Function of Molecular Structure</u>** Hydrolysis of an organic molecule occurs when a molecule (R-X) reacts with water (H_2O) to form a new carbon-oxygen bond after the carbon-X bond is cleaved (2,3). Mechanistically, this reaction is referred to as a nucleophilic substitution reaction, where X is the leaving group being replaced by the incoming nucleophilic oxygen from the water molecule. The leaving group, X, must be a molecule other than carbon because for hydrolysis to occur, the R-X bond cannot be a carbon-carbon bond. The carbon atom lacks sufficient electronegativity to be a good leaving group and carbon-carbon bonds are too stable (high bond energy) to be cleaved by nucleophilic substitution. Thus, hydrocarbons, including alkenes, are not subject to hydrolysis (3) and this fate process will not contribute to the degradative loss of chemical components in this category from the environment. Under strongly acidic conditions the carbon-carbon double bond found

	in alkenes, such as those in the High Benzene Naphthas Category, will react with water by an addition reaction mechanism (2). The reaction product is an alcohol. This reaction is not considered to be hydrolysis because the carbon-carbon linkage is not cleaved and because the reaction is freely reversible (3). Substances that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (4). The substances in the High Benzene Naphthas Category are primarily olefins that contain at least one double bond (alkenes). The remaining chemicals are saturated hydrocarbons (alkanes). These two groups of chemicals contain only carbon and hydrogen. As such, their molecular structure is not subject to the hydrolytic mechanism discussed above. Therefore, chemicals in the High Benzene Naphthas Category have a very low potential to hydrolyze, and this degradative process will not contribute to their removal in the environment. **References** 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The High Benzene Naphthas Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA. 2. Gould, E.S. (1959), Mechanism and Structure in Organic Chemistry, Holt, Reinhart and Winston, New York, NY, USA. 3. Harris, J.C. (1982), "Rate of Hydrolysis," Chapter 7 in: W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, NY, USA. 4. Neely, W. B. 1985. Hydrolysis. In: W. B. Neely and G. E. Blau, eds. Environmental Exposure from Chemicals. Vol I., pp. 157-173. CRC Press, Boca Raton, FL, USA.
Reliability:	These data represent a key study for characterizing the potential of substances in the High Benzene Naphthas Category to undergo hydrolysis.
Reference:	American Chemistry Council, Olefins Panel. 2003. Hydrolysis High Benzene Naphthas Category. Rosslyn, VA, USA.
Other (source):	American Chemistry Council, Olefins Panel (Prepared 7/03)

* Other TS is a selection option under the Test Substance pick list that is in the IUCLID entry field for Hydrolysis. Selecting this option refers the reader to information in the test substance "freetext" field to which the CAS numbers can be added.

HIGH BENZENE NAPHTHAS ROBUST SUMMARY

Photodegradation (Direct)

Test Substance*:	Other TS [CAS # 64741-99-7; 64742-49-0; 64742-73-0; 64742-83-2; 64742-91-2; 67891-79-6; 67891-80-9; 68410-97-9; 68475-70-7; 68476-45-9; 68526-77-2; 68606-10-0; 68606-28-0; 68921-67-5; 68955-29-3; 68956-52-5; 68956-70-7; 69013-21-4; 8030-30-6]
Method/Guideline:	Other: Technical discussion
Year (guideline):	Not applicable
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Type (air, soil, water, other):	Water
Light Source:	Not applicable
Light Spectrum: • **Wave length value (upper/lower)**	Not applicable
Relative Intensity:	Not applicable
Test Substance Spectrum:	Not applicable
Test Conditions: • **Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol**	Not applicable
Direct Photolysis:** • **Results: half-life, % degradation, quantum yield**	**Summary** In the environment, direct photolysis will not significantly contribute to the degradation of constituent chemicals in the High Benzene Naphthas Category. The High Benzene Naphthas Category includes ten process streams: • **Pyrolysis Gasoline** • **Pyrolysis C6 Fraction** • **Pyrolysis C6-C8 Fraction** • **Pyrolysis C5-C6 Fraction** • **Hydrotreated C6 Fraction** • **Hydrotreated C6-C7 Fraction** • **Hydrotreated C6-C8 Fraction** • **Quench Loop Pyrolysis Oil and Compressor Oil** • **Recovered Oil from Waste Water Treatment**

	• **Extract from Benzene Extraction** Nineteen CAS numbers (see Test Substance) identify products derived from these process streams. As discussed below, the reaction process involved in direct photolysis occurs when sufficient light energy excites a molecule to the degree that a structural transformation occurs. In general, substances in this category do not contain component chemicals that will undergo direct photolysis. **The High Benzene Naphthas Category** A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity. The category includes hydrocarbon product streams associated with the ethylene industry that contain significant levels of benzene, generally with a benzene content greater than 10% and averaging about 55%. In some cases, petroleum refinery streams may be combined with intermediate streams from the ethylene unit and co-processed to produce these products. This grouping of CAS numbers represents hydrocarbon streams with a carbon number distribution that is predominantly C5-C11, through components boiling at 650°F or higher. That is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated High Benzene Naphthas. The definitions found in the TSCA Chemical Substance Inventory for the CAS numbers included in this group are vague with respect to composition. Therefore, it is possible to find that the same CAS number is correctly used to describe different streams (compositions) or that two or more different CAS numbers are used to describe the same stream (composition or process). More information on the High Benzene Naphthas Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). The plan is available on the U.S. Environmental Protection Agency website under the HPV Chemical Program. A brief description of the production and composition of the ten process streams in this category are: • **Pyrolysis Gasoline** (Pygas) consists predominantly of C5+ hydrocarbons produced by the ethylene cracking furnaces. Typically the stream is derived from (1) the bottoms product from the debutanizer, (2) oils separated from furnace effluent quench systems, and (3) “drips” or condensate resulting from compression of the cracked gas. The oils from the quench systems and the “drips” may be stabilized to remove lights before blending with Pygas from the other sources. Depending on the plant configuration, Pygas may contain all of these intermediate streams, or the quench oils and stabilized drips may be transferred as separate streams. Low concentrations (e.g. 3% total) of C4 and lighter hydrocarbons may be present in the stream. A detailed analysis of Pygas may identify 60 or more hydrocarbon components or component groups, primarily unsaturated hydrocarbons and aromatics. Benzene, toluene, and dicyclopentadiene together may account for more than 50% of a Pygas stream and typically no other single component is present at a level greater than about 5%. The benzene concentration of

	Pygas is typically about 40% and the reported values range from 15 to 62%. The concentrations of individual hydrocarbon components in Pygas vary depending on the type of feedstock used by the ethylene plant, the mode of operation of the cracking furnaces (i.e. severity) and the ethylene process configuration. One non-typical Pygas stream is reported to contain vinylacetate at a concentration of up to about 10%. Vinylacetate is not typically found in ethylene process streams. • **Pyrolysis Gasoline Fractions (C5-C6, C6, and C6-C8 Fractions)** are separated by distillation into various boiling-point range fractions as intermediates in preparation for further processing. In some cases, petroleum refinery streams such as a C6 reformate fraction are combined with the pyrolysis gasoline prior to this separation. Similar to the situation for Pygas, the composition of these fractions vary depending on the ethylene process feedstock and the other operating variables. **4.** **Pyrolysis C5-C6 Fraction** has a carbon number distribution that is predominantly C5 to C6. One typical composition for this stream is reported as 70% benzene and 10% pentenes. **5.** **Pyrolysis C6 Fraction** has a carbon number distribution that is predominantly C6. Reported compositions vary from 35 to 77% benzene, 0.5 to 5% toluene with the balance primarily C6 non-aromatics, which are expected to be largely unsaturates. **6.** **Pyrolysis C6-C8 Fraction** has a carbon number distribution that is predominantly C6 to C8. The reported compositions range from 30 to 80% benzene, 15 to 25% toluene and 3 to 23% C8 aromatics. • **Hydrotreated Pyrolysis Fractions (C6, C6-C7, and C6-C8 Fractions)** are Pyrolysis gasoline or distillate fractions of pyrolysis gasoline that are treated with hydrogen over catalyst to saturate or partially saturate diolefins and/or olefins. In some cases, petroleum refinery streams such as a C6 reformate fraction are combined with the pyrolysis gasoline prior to this step. The hydrogenation process may be either one-stage or two-stage. The one-stage process is typically a liquid-phase process where the primary objective is to selectively convert diolefins to mono-olefins and to convert vinyl aromatics, for example, styrene to ethylbenzene. The second stage in a two-stage hydrogenation process is typically a vapor-phase, more severe hydrogenation that converts essentially all of the contained olefins to saturated hydrocarbons. A pygas fraction that will be processed by extraction or extractive distillation to produce high purity aromatics (benzene, toluene, or xylenes) is subjected to two-stage hydrogenation. Pygas fractions may be forwarded to hydrodealkylation units (less common) for benzene production after one-stage of hydrogenation. Hydrotreated Pyrolysis fractions may be the result of either one- or two-stage hydrogenation. 4. **Hydrotreated C6 Fraction** is very similar to the Pyrolysis C6 fraction except that the non-aromatics present in the hydrotreated stream are essentially all saturates. The reported composition for the Hydrotreated C6 stream indicates typical benzene content of

	75%. 5. **Hydrotreated C6-C7 Fraction** has a carbon number distribution that is predominantly C6-C7 and the reported values indicate 40 to 70% benzene, and 3 to 15% toluene. 6. **Hydrotreated C6-C8 Fraction** has a reported typical composition of 40 to 60% benzene, 10 to 25% toluene, and 3 to 10% C8 aromatics. • **Quench Loop Pyrolysis Oil and Compressor Oil** (Pyoil) represents higher boiling hydrocarbons that condense in the water quench system of an ethylene plant, typically at an ethylene unit cracking ethane, propane or butane. The stream can also include liquids collected at the cracked gas compressor knock out drums, which may include compressor injection oil. The carbon number distribution for Pyoil is C4 (or even lower) through heavier hydrocarbons such as naphthalene or even heavier. The reported typical composition includes 10 to 22% benzene and 5 to 11% toluene. • **Recovered Oil from Wastewater Treatment** can be expected to be of variable composition and made up largely of the components found in Pygas. No composition data or process specific information has been reported. Typically, water streams at ethylene units are processed to separate hydrocarbons from the water so that the water can be reused to generate steam for process-contact use (dilution steam for the cracking furnaces) or so that excess water can be forwarded to treatment prior to discharge or reuse. Water processing typically includes mechanical and gravity separation and steam or gas stripping. Hydrocarbons separated from the water in these systems are not usually isolated from the process. However, at least in one case, the Recovered Oil from Wastewater Treatment has been reported as an isolated intermediate. • **Extract from Benzene Extraction** are hydrotreated pyrolysis fractions containing aromatics (most commonly benzene or benzene and toluene) which are typically charged to extraction or extractive distillation units where the mixed aromatics are recovered. The carbon number distribution for this stream is predominantly C6 to C8. A reported typical concentration indicates 60 to 75% benzene, 25 to 40% toluene and 0 to 1% xylenes. **<u>Photolysis of Hydrocarbons</u>** The direct photolysis of an organic molecule occurs when it absorbs sufficient light energy to result in a structural transformation (2). The reaction process is initiated when light energy in a specific wavelength range elevates a molecule to an electronically excited state. However, the excited state is competitive with various deactivation processes that can result in the return of the molecule to a non excited state. The absorption of light in the ultra violet (UV)-visible range, 110-750 nm, can result in the electronic excitation of an organic molecule. Light in this range contains energy of the same order of magnitude as

covalent bond dissociation energies (2). Higher wavelengths (e.g. infrared) result only in vibrational and rotational transitions, which do not tend to produce structural changes to a molecule.

The stratospheric ozone layer prevents UV light of less than 290 nm from reaching the earth's surface. Therefore, only light at wavelengths between 290 and 750 nm can result in photochemical transformations in the environment (2). Although the absorption of UV light in the 290-750 nm range is necessary, it is not always sufficient for a chemical to undergo photochemical degradation. Energy may be re-emitted from an excited molecule by mechanisms other than chemical transformation, resulting in no change to the parent molecule.

A conservative approach to estimating a photochemical degradation rate is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by the molecule (3). Saturated hydrocarbons do not absorb light above 200 nm. Some characteristic absorbance maxima (λ_{max}) and associated molar absorptivities (ε) for selected unsaturated hydrocarbons are shown below (2):

	λ below 290 nm		**λ above 290 nm**	
Hydrocarbon	λ_{max}	ε	λ_{max}	ε
Ethylene	193	10,000	-	-
Benzene	255	215	-	-
Styrene	244	12,000	-	-
	282	450		
Naphthalene	221	100,000	311	250
	270	5,000		

Olefins with one double bond, or two conjugated double bonds, which constitute the majority of the chemicals in the High Benzene Naphthas category, do not absorb appreciable light energy above 290 nm. The absorption of UV light to cause cis-trans isomerism about the double bond of an olefin occurs only if it is in conjugation with an aromatic ring (2).

Products in the High Benzene Naphthas Category do not contain component molecules that will undergo direct photolysis. Therefore, this fate process will not contribute to a measurable degradative removal of chemical components in this category from the environment.

References

1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The High Benzene Naphthas Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. Virginia, USA.

2. Harris, J. C. 1982. "Rate of Aqueous Photolysis," Chapter 8 in: W. J. Lyman, W. F. Reehl, and D. H. Rosenblatt, eds., Handbook of Chemical Property Estimation Methods, McGraw-Hill Book Company, New York, USA.

3. Zepp, R. G. and D. M. Cline. 1977. Rates of Direct Photolysis in the Aqueous Environment, Environ. Sci. Technol., 11:359-366.

Indirect Photolysis:** • **Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life**	Not applicable
Degradation Products:** • **Note: Identification, concentration**	Unknown
Test Substance:	The High Benzene Naphthas Category includes the following CAS numbers: 64741-99-7 Extracts, petroleum, light naphtha solvent 64742-49-0 Naphtha, petroleum, hydrotreated light 64742-73-0 Naphtha, petroleum, hydrodesulfurized light 64742-83-2 Naphtha, petroleum, light steam-cracked 64742-91-2 Distillates, petroleum, steam-cracked 67891-79-6 Distillates, petroleum, heavy aromatic 67891-80-9 Distillates, petroleum, light aromatic 68410-97-9 Distillates, petroleum, light distillate hydrotreating process, low-boiling 68475-70-7 Aromatic hydrocarbons, C6-8, naphtha-raffinate pyrolyzate-derived 68476-45-9 Hydrocarbons, C5-10 aromatic concentration, ethylene-manufacture-by-product 68526-77-2 Aromatic hydrocarbons, ethane cracking scrubber effluent and flare drum 68606-10-0 Gasoline, pyrolysis, debutanizer bottoms 68606-28-0 Hydrocarbons, C5 and C10-aliphatic and C6-8-aromatic 68921-67-5 Hydrocarbons, ethylene-manufacture-by-product distillation residues 68955-29-3 Distillates, petroleum, light thermal cracked, debutanized aromatic 68956-52-5 Hydrocarbons, C4-8 68956-70-7 Petroleum products, C5-12, reclaimed, wastewater treatment 69013-21-4 Fuel oil, pyrolysis 8030-30-6 Naphtha
Conclusion:	Not applicable
Reliability:	These data represent a key study for characterizing the potential of substances in the High Benzene Naphthas Category to undergo direct photodegradation.
Reference:	American Chemistry Council, Olefins Panel. 2003. Photodegradation (Direct): High Benzene Naphthas Category. Rosslyn, VA, USA.
Other (source):	American Chemistry Council, Olefins Panel (Prepared 7/03)

* Other TS is a selection option under the Test Substance pick list that is in the IUCLID entry field for Photodegradation (Direct). Selecting this option refers the reader to information in the test substance "freetext" field to which the CAS numbers can be added.

HIGH BENZENE NAPHTHAS ROBUST SUMMARY

Photodegradation (Indirect)

Test Substance*:	Other TS [CAS # 64741-99-7; 64742-49-0; 64742-73-0; 64742-83-2; 64742-91-2; 67891-79-6; 67891-80-9; 68410-97-9; 68475-70-7; 68476-45-9; 68526-77-2; 68606-10-0; 68606-28-0; 68921-67-5; 68955-29-3; 68956-52-5; 68956-70-7; 69013-21-4; 8030-30-6]
Method/Guideline:	Calculated values using AOPWIN version 1.89, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
GLP (Y/N):	Not applicable
Year (study performed):	Not applicable
Type (air, soil, water, other):	Not applicable
Light Source:	Sunlight
Light Spectrum: • **Wave length value (upper/lower)**	Natural sunlight
Relative Intensity:	1
Test Substance Spectrum:	Not applicable
Test Conditions: • **Note: Concentration, temperature, test system type, replication, deviations from guideline or protocol**	Indirect photodegradation, or atmospheric oxidation potential, is based on the structure-activity relationship methods developed by R. Atkinson. Temperature: 25°C Sensitizer: OH radical Concentration of Sensitizer: 1.5 E^6 OH radicals/cm^3
Direct Photolysis:** **Results: half-life, % degradation, quantum yield**	Not applicable

Indirect Photolysis:** • **Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life**	**The High Benzene Naphthas Category** High Benzene Naphthas Category substances arise from production processes associated with ethylene manufacturing. The 19 CAS numbers are used to describe the ten process streams arising from the ethylene process and other associated manufacturing processes. The category includes hydrocarbon product streams associated with the ethylene industry that contain significant levels of benzene, generally with a benzene content greater than 10% and averaging about 55%. Commercial substances in this category consist of both high purity hydrocarbons and complex hydrocarbon reaction products with a carbon number distribution that is predominantly C5-C11. That is why this group is considered a category for purposes of the High Production Volume (HPV) Chemical Program, and designated High Benzene Naphthas. The 12 chemicals selected to represent the atmospheric oxidation potential of this category are C5-C10 hydrocarbons that can be found in substances identified by the 19 CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, and olefinic process (distillation) knowledge. **Atmospheric Oxidation of Hydrocarbons** In the environment, organic chemicals emitted into the troposphere are degraded by several important transformation processes. The dominant transformation process for most compounds is the daylight reaction with hydroxyl (OH-) radicals (Atkinson, 1988, 1989). The rate at which an organic compound reacts with OH-radicals is a direct measure of its atmospheric persistence (Meylan and Howard, 1993). AOPWIN estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The rate constants estimated by the program are then used to calculate atmospheric half-lives for organic compounds based upon average atmospheric concentrations of hydroxyl radicals. Since the reactions only take place in the presence of sunlight, the atmospheric half-lives are normalized for a 12-hour day.

Indirect Photolysis: (cont'd)** **Results: type of sensitizer, concentration of sensitizer, rate constant, % degradation, half-life**	Chemical / Calculated* half-life (hrs) / OH- Rate Constant (cm^3/molecule-sec) Isoprene 1.2 105.1 E^{-12} n-pentane 31.7 4.0 E^{-12} 1,3-cyclopentadiene 0.9 142.6 E^{-12} Isohexane 22.4 5.7 E^{-12} n-hexane 23.5 5.5 E^{-12} methylcyclopentane 22.7 5.7 E^{-12} benzene 65.8 1.9 E^{-12} toluene 24.6 5.2 E^{-12} m-xylene 9.5 13.6 E^{-12} styrene 4.6 28.1 E^{-12} dicyclopentadiene 1.1 119.2 E^{-12} naphthalene 5.9 21.6 E^{-12} * Atmospheric half-life values are based on a 12-hr day. More information on the High Benzene Naphthas Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (Olefins Panel, 2001). References: 1. Atkinson, R. 1988. Estimation of gas-phase hydroxyl radical rate constants for organic chemicals. *Environ. Toxicol. Chem*. **7**:435-442. 2. Atkinson, R. 1989. Kinetics and mechanisms of the gas-phase reactions of the hydroxyl radical with organic compounds. J. Phys. Chem. Ref. Data Monograph No. 1, Amer. Inst. Physics & Amer. Chem. Soc., NY. 3. Meylan, W.M. and P.H. Howard. 1993. Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. *Chemosphere* **12**:2293-2299. 4. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The High Benzene Naphthas Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Degradation Products:** • **Note: Identification, concentration**	Unknown
Test Substance:	The High Benzene Naphthas Category includes the following CAS numbers: 64741-99-7 Extracts, petroleum, light naphtha solvent 64742-49-0 Naphtha, petroleum, hydrotreated light 64742-73-0 Naphtha, petroleum, hydrodesulfurized light

	64742-83-2 Naphtha, petroleum, light steam-cracked 64742-91-2 Distillates, petroleum, steam-cracked 67891-79-6 Distillates, petroleum, heavy aromatic 67891-80-9 Distillates, petroleum, light aromatic 68410-97-9 Distillates, petroleum, light distillate hydrotreating process, low-boiling 68475-70-7 Aromatic hydrocarbons, C6-8, naphtha-raffinate pyrolyzate-derived 68476-45-9 Hydrocarbons, C5-10 aromatic concentration, ethylene-manufacture-by-product 68526-77-2 Aromatic hydrocarbons, ethane cracking scrubber effluent and flare drum 68606-10-0 Gasoline, pyrolysis, debutanizer bottoms 68606-28-0 Hydrocarbons, C5 and C10-aliphatic and C6-8-aromatic 68921-67-5 Hydrocarbons, ethylene-manufacture-by-product distillation residues 68955-29-3 Distillates, petroleum, light thermal cracked, debutanized aromatic 68956-52-5 Hydrocarbons, C4-8 68956-70-7 Petroleum products, C5-12, reclaimed, wastewater treatment 69013-21-4 Fuel oil, pyrolysis 8030-30-6 Naphtha
Conclusion:	Atmospheric oxidation via hydroxyl radicals can be a significant route of degradation for products in this category. Based on calculated values, products in this category can have an atmospheric half-life range of 0.9 to 65.8 hours as a result of indirect photolysis by hydroxyl radical attack.
Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by AOPWIN. The data represent a potential atmospheric half-life range for substances represented by the 19 CAS numbers under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the High Benzene Naphthas Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for atmospheric half-life range based on constituent data.
Reference:	Meylan, M., SRC 1994-1999. AOPWIN is contained in the computer program EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.
Other (source):	American Chemistry Council, Olefins Panel (Prepared 10/03)

* Other TS is a selection option under the Test Substance pick list that is in the IUCLID entry field for Photodegradation (Indirect). Selecting this option refers the reader to information in the test substance "freetext" field to which the CAS numbers can be added.
** In IUCLID, provide additional discussion if needed in the results free text

HIGH BENZENE NAPHTHAS ROBUST SUMMARY

Partition Coefficient

Test Substance*:	Other TS [CAS # 64741-99-7; 64742-49-0; 64742-73-0; 64742-83-2; 64742-91-2; 67891-79-6; 67891-80-9; 68410-97-9; 68475-70-7; 68476-45-9; 68526-77-2; 68606-10-0; 68606-28-0; 68921-67-5; 68955-29-3; 68956-52-5; 68956-70-7; 69013-21-4; 8030-30-6]
Method/Guideline:	Calculated values using KOWWIN version 1.65, a subroutine of the computer program EPIWIN version 3.04
Year (guideline):	1999
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: • **Note: Concentration prep., vessel type, replication, test conditions.**	Octanol / Water Partition Coefficient is calculated by the KOWWIN subroutine, which is based on an atom/fragment contribution method of W. Meylan and P. Howard in "Atom/fragment contribution method for estimating octanol-water partition coefficients". 1995. *J. Pharm. Sci*. 84:83-92.
Results: **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Calculated and measured log K_{ow} data for representative constituents of the High Benzene Naphthas Category are listed below. The data identify a potential log K_{ow} range for substances represented by the 19 CAS numbers under Test Substance. Substances in this category do not have a specific log K_{ow} value. Actual log K_{ow} ranges for substances in this category will vary dependent on their constituent composition. Commercial substances in this category consist of both high purity hydrocarbons and complex hydrocarbon reaction products with a carbon number distribution that is predominantly C5-C11. The 12 chemicals selected to represent the log K_{ow} range of this category are C5-C10 hydrocarbons that can be found in substances identified by the 19 CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, and olefinic process (distillation) knowledge.

Results: (continued) **Units/Value:** **Note: Deviations from protocol or guideline, analytical method.**	Substance Constituent — Calculated log K_{ow} @ 25°C — Measured* log K_{ow} @ 25°C Isoprene 2.58 2.42 n-pentane 2.80 3.39 1,3-cyclopentadiene 2.25 na Isohexane 3.21 3.60 n-hexane 3.29 3.90 methylcyclopentane 3.10 3.37 benzene 1.99 2.13 toluene 2.54 2.73 m-xylene 3.09 3.20 styrene 2.89 2.95 dicyclopentadiene 3.16 na naphthalene 3.17 3.30 * Experimental values from EPIWIN database. na = not available The data represent a potential log K_{ow} range for substances represented by the 19 CAS numbers under Test Substance.
Test Substance:	The High Benzene Naphthas Category includes the following CAS numbers: 64741-99-7 Extracts, petroleum, light naphtha solvent 64742-49-0 Naphtha, petroleum, hydrotreated light 64742-73-0 Naphtha, petroleum, hydrodesulfurized light 64742-83-2 Naphtha, petroleum, light steam-cracked 64742-91-2 Distillates, petroleum, steam-cracked 67891-79-6 Distillates, petroleum, heavy aromatic 67891-80-9 Distillates, petroleum, light aromatic 68410-97-9 Distillates, petroleum, light distillate hydrotreating process, low-boiling 68475-70-7 Aromatic hydrocarbons, C6-8, naphtha-raffinate pyrolyzate-derived 68476-45-9 Hydrocarbons, C5-10 aromatic concentration, ethylene-manufacture-by-product 68526-77-2 Aromatic hydrocarbons, ethane cracking scrubber effluent and flare drum 68606-10-0 Gasoline, pyrolysis, debutanizer bottoms 68606-28-0 Hydrocarbons, C5 and C10-aliphatic and C6-8-aromatic 68921-67-5 Hydrocarbons, ethylene-manufacture-by-product distillation residues 68955-29-3 Distillates, petroleum, light thermal cracked, debutanized aromatic 68956-52-5 Hydrocarbons, C4-8 68956-70-7 Petroleum products, C5-12, reclaimed, wastewater treatment 69013-21-4 Fuel oil, pyrolysis 8030-30-6 Naphtha High Benzene Naphthas Category substances arise from production processes associated with ethylene manufacturing. The 19 CAS numbers are used to describe the ten process streams arising from the ethylene process and other associated

	manufacturing processes. The category includes hydrocarbon product streams associated with the ethylene industry that contain significant levels of benzene, generally with a benzene content greater than 10% and averaging about 55%. More information on the High Benzene Naphthas Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The High Benzene Naphthas Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	The calculated log K_{ow} for some representative constituents that are present in the category streams vary from 1.99 to 3.29 @ 25°C. The measured log K_{ow} of these same constituents vary from 2.13 to 3.90 @ 25°C. Although this does not define the actual log K_{ow} of the category streams, it offers an indication of a range that might be expected to encompass the log K_{ow} of these complex streams with variable compositions. Log K_{ow} values outside of these ranges may be possible for some category streams.
Reliability:	(2) Reliable with restrictions The results include calculated data based on chemical structure as modeled by EPIWIN and measured data for specific chemicals as cited in the EPIWIN database. The data represent a potential log K_{ow} range for substances represented by the 19 CAS numbers under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the High Benzene Naphthas Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for log K_{ow} range based on constituent data.
Reference:	EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA. (Log K_{ow} values were calculated by the KOWWIN subroutine and measured data came from the database in the computer program.)
Other (source):	American Chemistry Council, Olefins Panel (Prepared 7/03)

* Other TS is a selection option under the Test Substance pick list that is in the IUCLID entry field for Partition Coefficient. Selecting this option refers the reader to information in the test substance "freetext" field to which the CAS numbers can be added.

HIGH BENZENE NAPHTHAS ROBUST SUMMARY

Transport / Distribution (Fugacity)

Test Substance*:	Other TS [CAS # 64741-99-7; 64742-49-0; 64742-73-0; 64742-83-2; 64742-91-2; 67891-79-6; 67891-80-9; 68410-97-9; 68475-70-7; 68476-45-9; 68526-77-2; 68606-10-0; 68606-28-0; 68921-67-5; 68955-29-3; 68956-52-5; 68956-70-7; 69013-21-4; 8030-30-6]
Method/Guideline:	Calculated according to Mackay Level I, EQC Model version 1.01
Year (guideline):	1997
Type (test type):	Not applicable
GLP:	Not applicable
Year (study performed):	Not applicable
Estimation Temperature:	25°C
Test Conditions: • **Note: Concentration prep., vessel type, replication, test conditions.**	The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. Physicochemical input values for the model were calculated using the EPIWIN Estimation v 3.04 program (1). Measured input values were also used where available and obtained from the EPIWIN database (1). Distribution data from the equilibrium model provide basic information on the potential partitioning behavior of chemicals between selected environmental compartments (i.e., air, water, soil, sediment, suspended sediment, biota). 1. EPIWIN. 1999. Estimation Program Interface for Windows, version 3.04. Syracuse Research Corporation, Syracuse, NY, USA.

Results:

Units/Value:

- **Note: Deviations from protocol or guideline, analytical method.**

Calculated partitioning data for representative constituents of the High Benzene Naphthas Category are listed below. The data identify a potential distribution for substances represented by the 19 CAS numbers under Test Substance. Actual distribution of substances in this category will vary dependent on their constituent composition.

Commercial substances in this category consist of both high purity hydrocarbons and complex hydrocarbon reaction products with a carbon number distribution that is predominantly C5-C11. The 12 chemicals selected to represent the boiling point range of this category are C5-C10 hydrocarbons that can be found in substances identified by the 19 CAS numbers. Constituents representing category members were selected on the basis of carbon number as identified by the category name, chemistry/structure, measured boiling point ranges for category substances, and olefinic process (distillation) knowledge.

The range of distribution data for constituent chemicals in each of the compartments can be used as an estimate of the partitioning behavior for category substances.

The following Mackay Level I model distribution values for representative constituents of substances in this category were determined using physicochemical input data calculated using the EPIWIN program:

	Calculated* Percent Distribution			
Chemical	Air	Water	Soil	Sediment
Isoprene	99.97	0.02	0.01	-
n-pentane	99.97	0.02	0.01	-
1,3-cyclopentadiene	99.93	0.06	0.01	-
Isohexane	99.96	0.02	0.02	-
n-hexane	99.95	0.02	0.02	-
methylcyclopentane	99.94	0.03	0.03	-
benzene	98.46	1.42	0.12	-
toluene	98.17	1.40	0.43	-
m-xylene	97.19	1.33	1.45	0.03
styrene	95.55	2.61	1.80	0.04
dicyclopentadiene	98.00	0.87	1.11	0.02
naphthalene	24.47	32.28	42.28	0.94

* Distribution values determined using calculated input data from EPIWIN program

Results: (cont'd) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Measured** Percent Distribution Isoprene 99.96 0.03 0.01 - n-pentane 99.99 0.01 - - 1,3-cyclopentadiene 99.93 0.06 0.01 - Isohexane 99.97 0.01 0.02 - n-hexane 99.96 - 0.04 - methylcyclopentane 99.95 0.02 0.03 - benzene 98.89 1.00 0.11 - toluene 98.80 0.81 0.39 - m-xylene 97.91 0.86 1.20 0.03 styrene 96.65 1.85 1.46 0.04 dicyclopentadiene 98.55 0.63 0.80 0.02 naphthalene 42.27 20.56 36.33 0.81 ** Distribution values determined using input data from the EPIWIN program experimental database
Test Substance:	The High Benzene Naphthas Category includes the following CAS numbers: 64741-99-7 Extracts, petroleum, light naphtha solvent 64742-49-0 Naphtha, petroleum, hydrotreated light 64742-73-0 Naphtha, petroleum, hydrodesulfurized light 64742-83-2 Naphtha, petroleum, light steam-cracked 64742-91-2 Distillates, petroleum, steam-cracked 67891-79-6 Distillates, petroleum, heavy aromatic 67891-80-9 Distillates, petroleum, light aromatic 68410-97-9 Distillates, petroleum, light distillate hydrotreating process, low-boiling 68475-70-7 Aromatic hydrocarbons, C6-8, naphtha-raffinate pyrolyzate-derived 68476-45-9 Hydrocarbons, C5-10 aromatic concentration, ethylene-manufacture-by-product 68526-77-2 Aromatic hydrocarbons, ethane cracking scrubber effluent and flare drum 68606-10-0 Gasoline, pyrolysis, debutanizer bottoms 68606-28-0 Hydrocarbons, C5 and C10-aliphatic and C6-8-aromatic 68921-67-5 Hydrocarbons, ethylene-manufacture-by-product distillation residues 68955-29-3 Distillates, petroleum, light thermal cracked, debutanized aromatic 68956-52-5 Hydrocarbons, C4-8 68956-70-7 Petroleum products, C5-12, reclaimed, wastewater treatment 69013-21-4 Fuel oil, pyrolysis 8030-30-6 Naphtha High Benzene Naphthas Category substances arise from production processes associated with ethylene manufacturing. The 19 CAS numbers are used to describe the ten process streams arising from the ethylene process and other associated

	manufacturing processes. The category includes hydrocarbon product streams associated with the ethylene industry that contain significant levels of benzene, generally with a benzene content greater than 10% and averaging about 55%. More information on the High Benzene Naphthas Category can be found in the American Chemistry Council, Olefins Panel test plan for this category (1). 1. Olefins Panel, HPV Implementation Task Group. 2001. High Production Volume (HPV) Chemical Challenge Program Test Plan For The High Benzene Naphthas Category. American Chemistry Council, Olefins Panel, HPV Implementation Task Group. VA, USA.
Conclusion:	The partitioning data represent a potential distribution range for substances in the 19 CAS numbers listed under Test Substance. Substances in the High Benzene Naphthas Category are calculated to partition primarily to air with a small percentage partitioning to water, soil, and sediment. Relatively high vapor pressure and high water solubility largely control the partitioning behavior of constituent chemicals in substances from this category. The input data used to run the EQC Level I model included estimated values calculated by the EPIWIN program based on chemical structure and measured data from the EPIWIN database. A comparison of the distribution data developed using either all calculated input values or measured values where data were available indicate a similar partitioning behavior and support the use of the dataset for chemicals without any measured data.
Reliability:	(2) Reliable with restrictions The input data used to run the EQC Level I model include calculated and experimental values available through the EPIWIN program. The data represent a potential environmental distribution range for substances with the 19 CAS numbers listed under Test Substance. This robust summary has a reliability rating of 2 because the data are not for specific substances in the High Benzene Naphthas Category, but rather for selected constituents. These selected constituents represent all substances defined by this category and as such, this robust summary represents a "key study" for distribution range based on constituent data.
Reference:	Mackay, D.A. DiGuardo, S. Paterson, and C. Cowan. EQC Model Version 1.01. 1997. Available from the Environmental Modeling Centre, Trent University, Canada.
Other (source):	American Chemistry Council, Olefins Panel (Prepared 7/03)

* Other TS is a selection option under the Test Substance pick list that is in the IUCLID entry field for Transport-Distribution. Selecting this option refers the reader to information in the test substance "freetext" field to which the CAS numbers can be added.

ATTACHMENT 1B

HIGH BENZENE NAPHTHAS ROBUST SUMMARIES:

BIODEGRADATION OF BENZENE

HIGH BENZENE NAPHTHAS ROBUST SUMMARY

Biodegradation

Test Substance:	CAS No. 71-43-2; Benzene
Method/Guideline:	OECD 301F
Year (guideline):	1993
Type (test type):	Ready Biodegradability, Manometric Respirometry Test
GLP:	Yes
Year (study performed):	2000
Inoculum:	Domestic activated sludge
Exposure Period:	28 days
Test Conditions: (FT - TC) • **Note: Concentration prep., vessel type, replication, test conditions.**	Activated sludge and test medium were combined prior to test material addition. Test medium consisted of glass distilled water and mineral salts (Phosphate buffer, Ferric chloride, Magnesium sulfate, Calcium chloride, EDTA). Test vessels were 500 mL dark glass bottles placed on a magnetic stirrer and electronically monitored for oxygen consumption. Test material and blanks were tested in triplicate, controls were tested in duplicate. Test material (benzene) concentration was 17mg/L. Sodium benzoate (positive control) concentration was 30mg/L. Toxicity control with benzene and Na Benzoate concentrations at 17 and 30 mg/L, respectively. Test temperature was 22 +/- 2 Deg C. All test vessels were stirred constantly for 28 days using magnetic stir bars and plates.
Results: (FT - RS) **Units/Value:** • **Note: Deviations from protocol or guideline, analytical method.**	Test material was readily biodegradable. Half-life was <2 weeks. By day 28, 63.0% degradation of the test material was observed. 10% biodegradation was achieved in less than 5 days, 50% biodegradation on approximately day 5. By day 5, >60% biodegradation of positive control was observed, which meets the guideline requirement. No excursions from the protocol were noted. Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test material as calculated using results of an elemental analysis of the test material.

Sample	% Degradation* (day 28)	Mean % Degradation (day 28)
Benzene	54, 72, 63	63
Na Benzoate	65, 75	70
Toxicity Control	59, 65	62

* replicate data

Conclusion: (FT - CL)	Test material was readily biodegradable. Half-life was <2 weeks
Reliability: (FT - RL)	(1) Reliable without restriction
Reference: (FT - RE)	Brixham Environmental Laboratory. 2001. OECD 301F, Ready biodegradability: Manometric respirometry. Study # AH0378/A.
Other (source): (FT - SO)	Olefins Panel, American Chemistry Council

* IUCLID field abbreviations include:
FT - Freetext
TC - Test Conditions
RS - Results
CL - Conclusion
RL - Reliability
RE - Reference
SO - Source

ROBUST SUMMARIES PART 3

HIGH BENZENE NAPHTHAS ROBUST SUMMARIES:

MAMMALIAN TOXICITY

ARE ALSO USED FOR PYROLYSIS C3+ AND C4+

Robust Summary: High Benzene Naphthas

Acute Toxicity

Test Substance	**Dripolene**. Yellow, homogeneous liquid, stable for 5 years at ambient temperature. (CRU #93329). Olefins Panel HVP Stream: Pyrolysis Gasoline. Typical composition ranges for Pyrolysis Gasoline are shown in Table 2 of the Test Plan.
Method	
Method/guideline followed	Not specified
Type (test type)	Acute, limit test
GLP	Yes
Year	1994
Species/Strain	Rat, Sprague-Dawley
Sex	Males and females
No. of animals per sex /dose	5
Vehicle	None
Route of administration	Oral gavage
Test Conditions	Sprague Dawley rats (180-350g) were individually housed in stainless steel suspended cages and fasted overnight prior to administration of 2g/kg neat dripolene. The study room was maintained at 68-72^{0}F with a relative humidity of 35-63% and a 12 hr light-dark cycle. Water and chow diet were available ad lib after dosing. Test article was administered once on day 1 by oral gavage through a blunted needle. Rats were observed for clinical signs approx. 30 min, 1hr, and 4hr, after dosing, and daily thereafter until sacrifice on day 15. Rats were checked once a day for mortality and moribundity. Observations were not made on weekends. Body wts were recorded prior to fasting and on days 1, 8 and 15.
Results	
LD_{50} with confidence limits.	The LD_{50} was not reached at 2g/kg. There were no deaths and all rats gained some weight during the study. Clinical signs noted in one or more rats were salivation, decreased activity, rales, lacrimation, chromodacryorrhea, ataxia, head shaking, chromorhinorrhea, miosis, slight tremors, mydriasis, hyperactivity, hypothermia, urogenital discharge, nasal discharge, decreased food consumption, decreased fecal output, vocalization, and decreased stool size. No gross pathological findings were noted at necropsy.
Remarks	
Conclusions (study author)	The LD_{50} was not reached at 2g/kg.
Data Quality	
Reliability	**1.** Reliable without restriction.
References	Rodriguez, S.C. and Dalbey, W.E. 1994. Acute oral toxicity of dripolene in Sprague Dawley Rats. Study #65642. Stonybrook Laboratories, Princeton, NJ. for Mobil Chemical Co., Edison, NJ.
Other	
Last changed	10/23/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: High Benzene Naphthas

Acute Toxicity

Test Substance	**Dripolene**. Yellow, homogeneous liquid, stable for 5 years at ambient temperature. (CRU #93329). Olefins Panel HVP Stream: Pyrolysis Gasoline. Typical composition ranges for Pyrolysis Gasoline are shown in Table 2 of the Test Plan.
Method	
Method/guideline followed	Not specified
Type (test type)	Acute, limit test
GLP	Yes
Year	1994
Species/Strain	Rabbit, New Zealand White
Sex	Males and females
No. of animals per sex/dose	3
Vehicle	None
Route of administration	dermal
Test Conditions	Rabbits, weighing at least 2kg, were individually housed in stainless steel suspended cages in a study room maintained at 69-72^{0}F with a relative humidity of 40-85% and a 12 hr light-dark cycle. Water and chow diet were available ad lib. The dorsal skin surface extending down from the front to rear legs and from left to right lower flanks was clipped free of hair the day prior to test article administration. Test article was spread evenly over the clipped area (approx. 10% of body surface area) at a dose of 2g/kg. A layer of 8-ply gauze was placed on the dorsal site, and a rubber dam sleeve was fitted snugly over the gauze pad and around the trunk. Edges of the dam were taped in place. An Elizabethan collar was affixed to the neck to prevent oral ingestion of test article and mechanical irritation of the test site. After 24 hrs, the collar and wrappings were removed and residual test article was wiped off. Body wts were recorded on days 1, 8 and 15. Rabbits were observed for toxicity at about 1 and 2 hr post-dose and daily thereafter on weekdays, through day 14. Observations for mortality/moribundity were made daily. Rabbits were sacrificed on day 15 and necropsies were performed.
Results	
LD_{50} with confidence limits.	The LD_{50} was not reached at 2g/kg. There were no deaths during the study and rabbits either gained some weight or remained at day 1 body wt. Signs that might have resulted from treatment in one or more rabbits were: decreased fecal output, decreased fecal pellet size, soft stool, and decreased food consumption. No gross pathological findings were noted at necropsy.
Remarks	
Conclusions	
(study author)	The LD_{50} was not reached at 2g/kg.
Data Quality	
Reliability	**1.** Reliable without restriction.
References	Rodriguez, S.C. and Dalbey, W.E. 1994. Dermal toxicity of dripolene in the New Zealand White rabbit. Study #65643. Stonybrook Laboratories, Princeton, NJ. for Mobil Chemical Co., Edison, NJ.
Other	
Last changed	10/23/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: High Benzene Naphthas

Acute Toxicity

Test Substance	**Hydrogenated Pyrolysis Gasoline** CAS# 68410-97-9. Clear liquid, aromatic odor. Olefins Panel HVP Stream: Hydrotreated C6-C8.
Method	
Method/guideline followed	Standard method (not referenced) with doses based on a limit test and range-finding study
Type (test type)	Acute LD50
GLP	Yes
Year	1984
Species/Strain	Rat, Fischer 344
Sex	Males and females
No. of animals per sex per dose	5
Vehicle	None
Route of administration	Oral
Test Conditions	Rats (99.9-134.0 g; 57 days old) were individually housed in screen-bottomed cages in a room with 70.6^{0}F temperature, relative humidity of 59% and a 12 hr light/dark cycle. Chow diet and tap water from an automatic watering system were available ad lib. Rats were fasted for 24 hours prior to dosing at 4.2, 4.6, 5.0, and 5.4g/kg and observed at 1 and 4 hrs after dosing on day 1, and daily thereafter, over 14 days for clinical signs, morbidity and mortality. Gross necropsies were performed on all rats. LD50 was calculated by Probit analysis.
Results	
LD_{50} with confidence limits.	LD50 = 5.17g/kg (95% confidence limits: 5.02-5.45g/kg) On day 1, males and females showed dose responsive increases in ataxia, harsh respiratory sounds, and a non-dose responsive increase in red ocular discharge.
Remarks	Soft feces were observed in treated males and females on day 2. Frequency of clinical signs decreased by day 3 and signs were absent by day 5. There were no changes in body weight gain among the groups. Male and female mortalities were combined to calculate an LD50. Mortality from a previously performed limit test, conducted at 5.0g/kg was combined with results from the 5.0g/kg dose in this definitive study, raising that group number to 20. Mortalities were: 0/10 at 4.2, and 4.6g/kg, 7/20 at 5.0g/kg, 7/10 at 5.4g/kg. Gross necropsies revealed red lungs, gas-filled stomach and intestine, mottled liver, discoloration of kidney, and opaque eyes in rats that died during the study. These observations, with the exception of opacity in the left eye of one 5.4g/kg female, were absent in rats sacrificed at study termination (day 15).
Conclusions (study author)	The acute median lethal dose (LD50) for Hydrogenated Pyrolysis Gasoline in male and female rats was 5.17g/kg. A descriptive classification of Practically Non-toxic for acute oral exposure was assigned.
Data Quality	
Reliability	**1.** Reliable without restrictions.
References	Rausina, G.A. 1984. Acute oral toxicity study in rats of hydrogenated pyrolysis gasoline. Proj. #2091. Gulf Life Sciences Center, Pittsburgh, PA
Other	
Last change	5/7/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: High Benzene Naphthas

Acute Toxicity

Test Substance	**Hydrogenated Pyrolysis Gasoline** CAS# 68410-97-9. Clear liquid, aromatic odor. Olefins Panel HVP Stream: Hydrotreated C6-C8.
Method	
Method/guideline followed	Standard method (not referenced)
Type (test type)	Acute LC50
GLP	Yes
Year	1984
Species/Strain	Rat, Fischer 344
Sex	Males and females
No. of animals per sex /dose	5
Vehicle	Filtered air
Route of administration	Inhalation
Test Conditions	Rats (8 wks. old, 100-172g at initiation) were individually housed in stainless steel, screen-bottomed cages in a room maintained at 73.0^{0}F (75.5^{0}F during exposure) temperature, relative humidity of 51% (40% during exposure) and a 12 hr light/dark cycle. Rats received chow diet and tap water ad lib, except during exposure. One group of 10 rats was exposed to aerosolized test article generated by a ball jet nebulizer for 4 hrs. A condensing flask was used to prevent large particles from entering the chamber. Actual average chamber concentration was 12,408ppm (range 8,642-17,371ppm) determined by gas chromatography. Particulate phase was negligible. Rats were observed for clinical signs at 1 and 4 hrs after dosing on day 1 and daily thereafter over 14 days, and for morbidity and mortality twice daily on weekdays, once daily on weekends. Body wt. was determined at initiation and on days 8 and 15. Gross necropsies were performed on all rats at termination on day 15.
Results	
LC_{50} with confidence limits.	LC50>12,408ppm
Remarks	There were no deaths during the study, no effects on body wt gain, and no gross alterations were seen at necropsy. Immediately after exposure, all rats exhibited lethargy, increased and labored respiration, and ocular discharge; most animals showed twitching and dry red material around nose/mouth. There were a few instances of harsh respiratory sounds, trembling, and perianal soiling. These clinical signs decreased in frequency by 4 hr post-exposure and disappeared by day 2.
Conclusions (study author)	No deaths occurred at the dose of 12,408ppm of test article, indicating a descriptive classification of Practically Non-toxic for acute inhalation exposure. Clinical signs noted immediately after exposure (increased/labored respiration, twitching, trembling, lethargy, ocular discharge) were not observed by day 2 and thereafter.
Data Quality	
Reliability	**1.** Reliable without restrictions.
References	Rausina, G.A. 1984. Acute inhalation toxicity study in rats of hydrogenated pyrolysis gasoline. Proj. #2092. Gulf Life Sciences Center, Pittsburgh, PA
Other	
Last change	Revised 7/27/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: High Benzene Naphthas

Genetic Toxicity - in Vitro

Test Substance	**Hydrogenated Pyrolysis Gasoline**, CAS #68410-97-9. clear liquid with aromatic odor, negligible solubility in water, contains <55.0% benzene, <25% toluene, <10% dimethyl benzene/xylene, <7% pentane, <7% ethylbenzene, <3% cyclohexane, <2% hexane. Olefins Panel HVP Stream: Hydrotreated C6-C8.
Test substance	
Method	
Method/guideline followed	Standard method per Ames et al
Type	Reverse mutation bacterial assay
System of testing	Salmonella typhimurium, Escherichia coli with and without metabolic activation
GLP	Yes
Year	1991
Species/Strain	S. typh. TA1535, TA1537, TA98, TA100; E. coli WP2(uvrA)
Metabolic activation	Yes
Species and cell type	Male Sprague Dawley rat liver (S9 fraction), Molecular Toxicology, Inc., Annapolis, MD
Quantity	20% S9 fraction in 0.5ml S9 mix/plate
Induced or not induced	Aroclor 1254 induced, rats given a single 500mg/kg ip dose
Concentrations tested	0, 33, 100, 333, 1000, 3333, 10,000µg/plate ± S9. All diluted in acetone (200mg/ml)
Statistical Methods	None specified. Test article considered mutagenic when it induces a reproductive, dose-related increase in number of revertants in one or more strains at 3 consecutive dose levels. A non-mutagen does not induce a dose-related increase in at least 2 independent tests.
Remarks for Test Conditions	Hydrogenated pyrolysis gasoline (HPG) was prepared in acetone immediately prior to use. At end of the study, an aliquot of the stock dilution was sent to PTRL West, Richmond, CA to confirm concentration. Salmonella (approx. 10^8cells/ml) were exposed to either test material or acetone in 3 plates/dose ± S9 by the plate incorporation method. Six dose levels from 33-10,000µg/plate were employed in both the range-finding trial using TA100 and the mutagenicity test with all strains of Salmonella and E. coli. Optimum level of S9 for the mutagenicity assay was determined by testing the highest non-toxic dose, 10,000µg per plate with metabolic activation systems containing 4, 20 or 80% S9 fraction. No noteworthy increases in revertants or cytotoxicity was observed at any S9 concentration; 20% S9 was used in the mutagenicity test. All plates were incubated at 37^0C for 48 hrs then revertant colonies were counted. Positive control compounds were: cultures-S9, sodium azide (5µg/plate) for TA1535, TA100; 9-aminoacridine (50µg/plate) for TA1537; 2-nitrofluorene (5µg/plate) for TA98; N-ethyl-N'-Nitro-N-Nitrosoguanidene (5ug/plate) for E. coli WP2, and cultures+S9, 2-anthramine (4µg/plate) for TA1535, TA1537, (2µg/plate) for TA98, TA100, and (20µg/plate) for E. coli WP2. Two independent assays were performed.
Results	
Genotoxic effects	HPG did not induce increases in number of revertant colonies and no toxicity was observed in any Salmonella strain or E. coli WP2 with or without 20% S9 metabolic activation in both studies. Positive control compounds performed appropriately.
Conclusions (contractor)	Hydrogenated pyrolysis gasoline is not mutagenic to bacteria under conditions of this assay.
Data Quality	
Reliabilities	**1**. Reliable without restriction

Reference	Riccio, E.S. and Stewart, K.R. 1991. Salmonella-Escherichia coli/microsome plate incorporation assay of Hydrogenated Pyrolysis Gasoline. SRI Study #2545-A03-91, Sponsor study #91-66. SRI International, Menlo Park, CA for Chevron Environmental Health Center, Richmond, CA
Other	
Last changed	5/7/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: High Benzene Naphthas

Genetic Toxicity - in Vitro

Test Substance	**Hydrogenated Pyrolysis Gasoline,** CAS #68410-97-9. clear liquid with aromatic odor. Composition, purity and stability referred to sponsor. Olefins Panel HVP Stream: Hydrotreated C6-C8.
Test substance	
Method	
Method/guideline followed	Standard method based on Cortesi et al (1983), Dunkel et al (1981), Reznikoff et al (1973)
Type	In vitro cell transformation
System of testing	Mouse embryo cells
GLP	Yes
Year	1984
Species/Strain	BALB/3T3-A31-1-1 from T. Kakunaga, National Cancer Inst., 1983
Metabolic activation	No
Species and cell type	NA
Quantity	NA
Induced or not induced	NA
Concentrations tested	Cytotoxicity: 8, 16, 32, 64, 128, 256, 512, 1024, 2048, and 5000µg/ml; Transformation: 100, 250, 500, 1500µg/ml, all diluted in 10% Pluronic® polyol F68 (prepared in deionized water, mol. wt. 8350, 80% hydrophilic).
Exposure period	2 days
Statistical Methods	None employed. Criteria for positive response were a two-fold increase in type III foci at the highest dose over vehicle control (at least 2 type III foci if vehicle control had none) with or without a dose related response, or a two-fold increase at two or more consecutive doses. Test is equivocal if two-fold increase occurred at any one level other than the highest acceptable dose.
Remarks for Test Conditions	Sufficient Hydrogenated Pyrolysis Gasoline (HPG) was weighed separately for each dose level, 0.40ml of 10% F68 added per ml of final volume and medium (Eagles MEM with 10% heat-inactivated fetal calf serum) added as required to achieve final volume for testing. Test preparations were mixed just prior to addition to cultures at 50µl to each 5 ml culture. All cultures were incubated at 37^0C in 5% CO2 enriched humidified atmosphere. For cytotoxicity, 2 cultures/dose group, 2 cultures for vehicle F68 or medium negative control were seeded with $1x10^4$ cells/plate in day 1, exposed on days 2-3, trypsinized and counted with a Coulter Model ZB on day 4 for at least 20% survival. For transformation, 15 cultures ($1x10^4$ cells/flask/dose group)) and two colony-forming cultures (100 cells/plate/dose group) were seeded on day 1, exposed on days 2-3 and culture medium changed on day 4. For transformation cultures, medium continued to be changed weekly to day 29. Positive control was 3-methylcholanthrene (1µg/ml). Colony forming cultures were fixed, stained, and counted visually on day 10 to determine cloning efficiency (avg. number colonies/plate ÷ 100 cells seeded). Transformation cultures were fixed and stained on day 29 for focus counting and evaluation. Transformation frequency = total type III foci ÷ total flasks/dose group.
Results	
Genotoxic effects	HPG induced toxicity in BALB/3T3 cells after two days exposure beginning at 128 µg/ml (45.4% relative survival) with relative survivals of 26.7, 25.6, 3.2 and 0% at 512, 1024, 2048 and 5000µg/ml, respectively. In the transformation assay, toxicity was seen at all dose levels (relative cloning efficiencies of 53.7, 67.8, 78.5 and 0% at 100, 250, 500 and 1500µg/ml). At 1500µg/ml, the highest dose level, HPG induced 5 Type III foci; no other dose levels produced a positive response. Transformation frequencies were 0.13, 0, 0, 0.07 and 0.36 for medium control, vehicle control, 100, 250, 500 and 1500µg/ml, respectively. Positive and negative controls gave appropriate responses.

Conclusions (contractor)	Hydrogenated Pyrolysis Gasoline induced transformation in BALB/3T3 cells under conditions of this assay. Cytotoxicity and impairment of cloning efficiency were also observed. The positive response was observed only at the highest dose level, a level that appeared to be too toxic for cells to recover and form colonies (0% relative colony forming efficiency)
Data Quality *Reliabilities*	**1.** Reliable without restriction
Reference	Brecher, S. 1984. Transformation test of Hydrogenated Pyrolysis Gasoline. Proj. #2098. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co, Houston, TX Cortesi, E. et al. 1983. Teratogenesis, Carcinogenesis, Mutagenesis 3: 101-110. Dunkel, V.A. et al. 1981. J. Nat'l Cancer Inst. 67: 1303-1315. Reznikoff, C.A. et al. 1973. Cancer Res. 3239-3249.
Other *Last changed*	Revised 8/27/2001 (Prepared by a contractor to the Olefins Panel).

Robust Summary - Group 5: High Benzene Naphthas

Genetic Toxicity - in Vitro

Test Substance	**Hydrogenated Pyrolysis Gasoline**, CAS #68410-97-9. clear liquid with aromatic odor. Composition, purity and stability referred to sponsor. Olefins Panel HVP Stream: Hydrotreated C6-C8.
Test substance	
Method	
Method/guideline followed	Standard method based on Williams et al (1977, 1982)
Type	In vitro mammalian DNA repair assay
System of testing	Unscheduled DNA synthesis (UDS) in primary hepatocyte cultures
GLP	Yes
Year	1984
Species/Strain	Fischer 344 male rat (10 wks old)
Metabolic activation	No
Species and cell type	NA
Quantity	NA
Induced or not induced	NA
Concentrations tested	8, 16, 32, 64, 128, 256, 512, 1024µg/ml diluted in 10% Pluronic F68 (prepared in deionized water, mol. wt 8350, 80% hydrophilic)
Exposure period	18 hrs.
Statistical Methods	None specified. Criteria for positive response are incorporation of radioactive precursor (^{3}H-thymidine) in cells that are not normally synthesizing DNA, indicating repair of damage. A positive response is defined as a mean net nuclear grain count at any treatment level that exceeds concurrent negative control by at least 6 grains/nucleus; negative control value must not exceed 5 grains. If this criterion is not met, a positive response can be identified if there is a significant difference ($p<0.01$) in % cells in repair at any dose level and negative control value. This indicator defines whether a small fraction of cells is undergoing repair (Casciano & Gaylor, 1983). A positive response need not be dose related.
Remarks for Test Conditions	Sufficient Hydrogenated Pyrolysis Gasoline (HPG) was weighed separately for each dose level, 0.40ml of 10% F68 added per ml of final volume and sufficient medium (Williams Medium E with 10% fetal bovine serum and insulin) added to achieve final volume. Test preparations were mixed just prior to addition at 20µl to each 2ml culture. The conc. of ^{3}H-thymidine (½ life 12.4 yrs.) used in these assays was 1mCi/ml. All cultures were incubated at 37^{0}C in 5% CO2 enriched humidified atmosphere. No range finding assay was performed. In the UDS assay, 2x10^5 cells/ml were seeded into coverslip cultures, exposed to ^{3}H-thymidine and test substance for 18 hours (3 cultures/dose level, 8 dose levels), untreated controls, vehicle F68 control and positive control, 2-acetyl aminofluorene (0.01µg/ml). Cells growing on coverslips were rinsed, fixed and glued to microscope slides on day 2. On day 3, slides were dipped in autoradiographic emulsion and stored in the dark at 2-8^{0}C. Autoradiographs were developed, stained and coverslipped on day 10. Numbers of grains overlying 50 randomly selected nuclei/slide were counted. The highest of 3 cytoplasmic grain counts/cell were subtracted and this number was divided by a conversion factor (unspecified) to obtain net nuclear grain count. Avg. net nuclear grain count/slide (sum of net nuclear grain count ÷ 50) and mean net nuclear grain count (avg. net nuclear grain count/slide ÷3) were calculated. In addition, % cells in repair were determined for each dose level.
Results	
Genotoxic effects	HPG induced toxicity in primary hepatocytes following 18 hr exposure that left too few cells for UDS analysis at doses of 512 and 1024µg/ml. HPG did not induce unscheduled DNA synthesis at any dose level with sufficient cells to be analyzed. Positive and negative controls gave appropriate responses.

Conclusions (contractor)	Hydrogenated Pyrolysis Gasoline did not induce unscheduled DNA synthesis in primary cultures of rat hepatocytes under conditions of this assay.
Data Quality *Reliabilities*	**2**. Reliable with restrictions. No table of cell counts/viability. No individual data to verify calculations and identify conversion factor. Statistical criteria are mentioned but method is not cited.
Reference	Brecher, S. 1984. Hepatocyte primary culture/DNA repair test of Hydrogenated Pyrolysis Gasoline. Proj. # 2097. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co., Houston, TX Williams, G.M. 1977. Cancer Res. 37: 1845-1851 Williams et al. 1977. In Vitro 13: 809-817 Williams et al. 1982. Mut. Res. 97:359-370 Casciano, D.A. and Gaylor, D.W. 1983. Mut. Res. 122:81-86
Other *Last changed*	5/7/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary - Group 5: High Benzene Naphthas

Genetic Toxicity - in Vivo

Test Substance	**Hydrogenated Pyrolysis Gasoline**, CAS #68410-97-9. Clear liquid with aromatic odor. Compositional analysis, purity and stability referred to sponsor. Olefins Panel HVP Stream: Hydrotreated C6-C8.
Remarks	
Method	
Method/guideline followed	None specified. Comparable to standard assay.
Type	Mammalian bone marrow erythrocyte micronucleus assay
GLP	Yes
Year	1984
Species	Mice
Strain	Crl:CD-1(ICR)BR Swiss
Sex	Male and female. Range-finding 2M, 2F (10 wks old)/group; 3 groups; Micronucleus test 10M, 10F (11 wks old)/group in 4 groups, 15M, 15F in one group.
Route of administration	Oral gavage
Doses/concentration levels	0, 0.5, 1.0, 2.0g/kg (2doses), 2.0g/kg (1 dose) undiluted
Exposure period	1 dose/day for 2 days: one group- 1 dose, 1 day only
Statistical methods	Values from treated groups for daily mean body weights, group means and std. dev. for polychromatic erythrocytes (PCEs) with micronuclei (MN) , and group mean ratios of PCE to normochromatic erythrocytes (NORMs) were calculated and compared with vehicle control values by Student's t-test. Positive response was indicated by statistically significant ($p<0.05$) increases in micronucleated PCE at any dose level with a dose related response evident. Results were considered equivocal if only one of these criteria was met.
Remarks for Test Conditions.	Animals in the range-finding study (2M, 2F/group), 3 treated groups (no control group) were given 1.25, 2.5, and 5.0g/kg neat hydrogenated pyrolysis gasoline (HPG) by gavage once each day for two days. Eighty percent of the dose level that produced ≤50% mortality was selected for the maximum dose in the micronucleus study. In the micronucleus study, three groups of mice were given undiluted HPG by oral gavage daily for two days at doses of 0.5, 1.0, 2.0g/kg, negative control mice were given corn oil (5g/kg). One-half of each treated group and negative control (5M, 5F) was killed on day 3 and the remainder on day 4. One group (15M, 15F), given 2.0 g/kg by gavage in a single dose for 1 day only, was killed on days 2, 3, 4 (5/sex/day). Positive control mice (4M, 4F) given cyclophosphamide (75 mg/kg) ip daily for 2 days were killed on day 3. Survival, body wt, and clinical signs were observed and recorded daily. Slides of femoral bone marrow smears were prepared, stained with May-Grunewald/Giemsa stain and examined microscopically. For each mouse, 1000 PCE and all associated mature erythrocytes (NORMs) were counted. Data collected included group mean body weights for each day, total PCEs, total NORMs, PCEs with MN, and NORMs with MN.
Results	
Genotoxic effects	
NOAEL (NOEL)	NOAELmortality = 1.0g/kg; NOELgenetics > 2.0g/kg (Assigned by reviewer)
LOAEL (LOEL)	In the range-finding study, half of the animals given HPG at conc of 5.0g/kg died on or before day 2. Gross necropsy of dead mice was unremarkable. In the micronucleus test, 1/10 males given 2.0g/kg (2 doses) died on day 2. No other mortality or significant wt changes were observed. Lethargy was observed among high dose mice. Surviving mice treated with HPG did not show any significant increase in micronucleus formation in PCE and no significant changes in ratio of PCE/NORM compared to negative controls. Negative and positive

	controls gave appropriate results.
Conclusions (study authors)	Oral treatment of mice with Hydrogenated Pyrolysis Gasoline for 1-2 days at doses up to 2.0g/kg/day had no effect on frequency of micronucleated polychromatic erythrocytes in bone marrow under these test conditions. HPG did not induce cytogenetic damage.
Data Quality *Reliabilities*	**1.** Reliable without restriction
References	Khan, S.H. 1984. Micronucleus test of Hydrogenated Pyrolysis Gasoline. Proj. #2096. Gulf Life Sciences Center, Pittsburgh, PA for Gulf Oil Chemicals Co., Houston, TX
Other *Last changed*	5/7/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary - Group 5: High Benzene Naphthas

Repeated Dose Toxicity

Test Substance	**Hydrogenated Pyrolysis Gasoline** CAS #68410-97-9, Clear liquid with aromatic odor. Olefins Panel HVP Stream: Hydrotreated C6-C8.
Remarks	
Method	
Method/guideline followed	Standard method, method not referenced
Test type	Subacute
GLP	Yes
Year	1984
Species	Rat
Strain	Fischer 344
Route of administration	Inhalation
Duration of test	8 days
Doses/concentration levels	0, 4869±470, 9137±917ppm±SD, actual exposure conc.
Sex	Males and females (5/sex/group)
Exposure period	6 hrs.
Frequency of treatment	once daily for 5 days (d1-5)
Control group and treatment	5M, 5F; filtered air
Post exposure observation period	2 days
Statistical methods	Body wt variance compared by Bartlett's test and one way analysis of variance. Group mean body wt compared either with Dunnett's test or a modified t-test to assess significance.
Test Conditions	Rats (9 wks old, 113-195g at initiation) were housed individually in stainless steel, screen-bottomed cages. Rooms were maintained at 72.2^{0}F (exposure chamber 75^{0}F) with relative humidity of 54% (exposure chamber 50%), and 12 hr light/dark cycle. Rats received chow diet and tap water ad lib throughout the study, except during exposure. Three groups of 10 rats (5M, 5F/group) each, were exposed to test article or air. Test article was aerosolized with a ball jet nebulizer; an in-line condensing flask was used to prevent large particles from entering the exposure chamber. Chamber concentration of test article was measured by gas chromatography. Rats were observed twice daily on weekdays and once daily on weekends for morbidity/mortality, and once daily for clinical signs immediately after exposure on days 1-5. Surviving rats were sacrificed on day 8. Gross necropsies were performed on all rats.
Results	
NOAEL (NOEL)	NOAEL< 4869ppm (estimated by reviewer)
LOAEL (LOEL)	LOAEL= 4869ppm (estimated by reviewer) based on clinical observations, reduced wt gain.
Remarks	Two rats (1M, 1F) from group 3 (9137ppm) died on day 2; one female from group 3 died during exposure on day 1. Rats in groups 2 and 3 showed ocular discharge throughout d1-5. Rats in group 2 showed increased respiratory rate and dry red material around nose and mouth. All rats in group 2 were lethargic and showed labored respiration. Many rats in group 3 were lethargic and exhibited twitching and harsh respiratory sounds during days 1-5. All rats in group 2 and all but one survivor in group 3 appeared normal on day 8. Group mean body wt was significantly decreased in a dose related manner. No test article related effects were seen at gross necropsy on day 8; the male rat that died during the study showed gas in the G.I. tract and red-tinged fluid in the stomach.
Conclusions	
(study authors)	Exposure to test article caused a significant decrease in group mean body wt of

	male and female rats of low and high dose groups that was correlated with exposure level. Three deaths occurred in the high dose group during exposure. Major clinical signs were lethargy, twitching, harsh respiratory sounds and ocular discharge. No gross alterations were found in rats surviving to sacrifice.
Quality	
Reliabilities	**1.** Reliable without restrictions
References	Rausina, G.A. 1984. Five-day repeated dose inhalation toxicity study in rats of Hydrogenated Pyrolysis Gasoline. Proj. #2099. Gulf Life Sciences Center, Pittsburgh, PA
Other	
Last changed	Revised 7/27/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary: High Benzene Naphthas

Acute Toxicity

Test Substance	**Pyrolysis gasoline (Rerun Tower Overheads**). Yellow, homogeneous liquid; 40% benzene, 26% C5, 13% toluene, 20% other. Test substance is described as a sample of a Pyrolysis Gasoline distillate fraction and is similar to Pyrolysis gasoline, a stream included in the test plan.
Method	
Method/guideline followed	Not specified
Type (test type)	Acute, limit test
GLP	Yes
Year	1994
Species/Strain	Rat, Sprague-Dawley
Sex	Males and females
No. of animals per sex /dose	5
Vehicle	None
Route of administration	Oral gavage
Test Conditions	Sprague Dawley rats (180-350g) were individually housed in stainless steel suspended cages and fasted overnight prior to administration of 2g/kg neat pyrolysis gasoline. The study room was maintained at 68-72^{0}F with a relative humidity of 35-63% and a 12 hr light-dark cycle. Water and chow diet were available ad lib after dosing. Test article was administered once on day 1 by oral gavage through a blunted needle. Rats were observed for clinical signs approx. 30 min, 1hr and 4hr, after dosing, and daily thereafter until sacrifice on day 15. Rats were checked once a day for mortality and moribundity. Observations were not made on weekends. Body wts were recorded prior to fasting and on days 1, 8 and 15.
Results	
LD_{50} with confidence limits.	The LD_{50} was not reached at 2g/kg. There were no deaths and all rats gained some weight during the study. Clinical signs noted in one or more rats were salivation, decreased activity, rales, lacrimation, chromodacryorrhea, ataxia, chromorhinorrhea, miosis, slight tremors, mydriasis, hyperactivity, hypothermia, urogenital discharge, nasal discharge, decreased food consumption, decreased fecal output, vocalization, and penile discharge. No gross pathological findings were noted at necropsy.
Remarks	
Conclusions	
(study author)	The LD_{50} was not reached at 2g/kg.
Data Quality	
Reliability	**1.** Reliable without restriction.
References	Rodriguez, S.C. and Dalbey, W.E. 1994. Acute oral toxicity of pyrolysis gasoline in Sprague Dawley Rats. Study #65636. Stonybrook Laboratories, Princeton, NJ. for Mobil Chemical Co., Edison, NJ.
Other	
Last changed	10/16/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary - Group 5: High Benzene Naphthas

Acute Toxicity

Test Substance	Pyrolysis gasoline (Rerun Tower Overheads). Yellow, homogeneous liquid; 40% benzene, 26% C5, 13% toluene, 20% other. Test substance is described as a sample of a Pyrolysis Gasoline distillate fraction and is similar to Pyrolysis gasoline, a stream included in the test plan.
Method	
Method/guideline followed	Not specified
Type (test type)	Acute, limit test
GLP	Yes
Year	1994
Species/Strain	Rabbit, New Zealand White
Sex	Males and females
No. of animals per sex /dose	3
Vehicle	None
Route of administration	dermal
Test Conditions	Rabbits, weighing at least 2kg, were individually housed in stainless steel suspended cages in a study room maintained at 69-72^{0}F with a relative humidity of 38-85% and a 12 hr light-dark cycle. Water and chow diet were available ad lib. The dorsal skin surface extending down from the front to rear legs and from left to right lower flanks was clipped free of hair the day prior to test article administration. Test article was spread evenly over the clipped area (approx. 10% of body surface area) at a dose of 2g/kg. A layer of 8-ply gauze was placed on the dorsal site, and a rubber dam sleeve was fitted snugly over the gauze pad and around the trunk. Edges of the dam were taped in place. An Elizabethan collar was affixed to the neck to prevent oral ingestion of test article and mechanical irritation of the test site. After 24 hrs, the collar and wrappings were removed and residual test article was wiped off. Body wts were recorded on days 1, 8 and 15. Rabbits were observed for toxicity at about 1 and 2 hr post-dose and daily thereafter on weekdays through day 14. Observations for mortality/moribundity were made daily. Rabbits were sacrificed on day 15 and necropsies were performed.
Results	
LD_{50} with confidence limits.	The LD_{50} was not reached at 2g/kg. There were no deaths during the study and rabbits either gained some weight or remained at day 1 body wt. Signs that might have resulted from treatment in one or more rabbits were: soft stool, decreased fecal pellet size, nasal discharge, and test site erythema. No gross pathological findings were noted at necropsy.
Remarks	
Conclusions	
(study author)	The LD_{50} was not reached at 2g/kg.
Data Quality	
Reliability	**1.** Reliable without restriction.
References	Rodriguez, S.C. and Dalbey, W.E. 1994. Dermal toxicity of pyrolysis gasoline in the New Zealand White rabbit. Study #65637. Stonybrook Laboratories, Princeton, NJ. for Mobil Chemical Co., Edison, NJ.
Other	
Last changed	10/16/2001 (Prepared by a contractor to the Olefins Panel)

Robust Summary - Group 5: High Benzene Naphthas

Genetic Toxicity - in Vitro

Test Substance	**Rerun Tower Overheads** from Olefins/Aromatics Plant (light thermal cracked naphtha) CAS # 64741-74-8. Straw colored liquid; 40% benzene, 26% C5, 13% toluene, 20% other. Test substance is described as a sample of a Pyrolysis Gasoline distillate fraction and is similar to Pyrolysis gasoline, a stream included in the test plan.
Test substance	
Method	
Method/guideline followed	Standard method based on Ames et al, 1975
Type	Reverse mutation bacterial assay
System of testing	Salmonella typhimurium with and without metabolic activation
GLP	Yes
Year	1981
Species/Strain	S. typhimurium TA 98, TA100, TA1535, TA1537, and TA1538.
Metabolic activation	Yes
Species and cell type	Sprague Dawley male rat liver (S9 fraction) from Litton Bionetics, Kensington, MD
Quantity	50ul S9 fraction in 0.5ml S9 mix/plate
Induced or not induced	Aroclor 1254-induced, rats were given a single ip 500mg/kg dose, 5 days prior to sacrifice.
Concentrations tested	0, 0.029, 0.094, 0.30, 0.97µl/plate –S9, and 0.094, 0.30, 0.97, and 3.1µl/plate + S9; samples diluted in dimethyl sulfoxide (DMSO). Negative control 50µl DMSO
Statistical Method	None. Criteria for a positive response were an increase in revertant colonies at least two-fold that of negative control at the lowest active dose, and a dose response curve. Positive results must be reproducible in an independent repeat assay.
Remarks for Test Conditions	Rerun tower overheads test solutions were prepared in DMSO immediately prior to use. Salmonella (Approx. 1.4-2x10^8 cells/ml) were exposed to either test solution or DMSO ±S9 by the preincubation method. Doses of 0.029-0.97µl/plate-S9 and 0.094-3.1µl/plate +S9 were determined by a pretest toxicity test in TA 100 and TA1537±S9 using incremental doses from 0.01-10µl/plate. Culture tubes containing 50µl test solution or DMSO, 0.1ml Salmonella and 0.5 ml phosphate buffer or S9 mix were combined and incubated with shaking (150 rpm) for 20 minutes at 37^{0}C. At the end of the preincubation period, top agar was added, mixed and cultures were overlaid on minimal agar plates, 3 plates/dose/strain. Plates were incubated at 37^{0}C for 48 hrs, then counted automatically (Biotran II) and background lawn evaluated by stereomicroscope. Positive control compounds were: -S9, 2-nitrofluorene (2-NF, 20µg/plate) for TA98 and TA1538; N-methyl-N'-nitro-N-nitrosoguanidine (MNNG, 2.0µg/plate) for TA100 and TA1535; 9-aminoacridine (9-AA, 25µg/plate) for TA1537; +S9 2-aminoanthracene (2µg/plate) for all strains except TA1537.
Results	
Genotoxic effects	The preliminary toxicity test exhibited severe toxicity at 10µl/plate with activation and at 3.1 and 10µl/plate without activation (individual data not shown). In the mutagenicity test, none of the 5 strains of Salmonella exhibited revertant frequencies substantially different from the solvent or spontaneous controls at any dose level with or without metabolic activation (e.g. TA98-S9: 16, 15, 12, 12, and 0 average revertants/plate and TA100-S9: 111, 115, 107, 94, and 0 at 0[DMSO], 0.029, 0.094, 0.30, and 0.97µl/plate, respectively: TA98+S9: 33, 26, 26, 22, and 0 revertants/plate, and TA100+S9: 128, 161, 128, 118, and 0 revertants/plate at 0[DMSO], 0.094, 0.30, 0.97 and 3.1µl/plate, respectively). Clearing of background lawn and microcolonies were observed at the maximum doses (0.97µl/plate-S9; 3.1µl/plate+S9). Positive control compounds (2 plates/strain) performed

	appropriately (-S9: MNNG 1906, 1883 revertants/plate in TA 100 and TA1535, respectively; 9-AA 586 revertants/plate in TA1537; 2-NF 2114, 1214 revertants/plate in TA98 and TA1538, respectively; and +S9 2- aminoanthracene 406-2307 revertants/plate for all strains except TA1537). The results of this assay indicate that rerun tower overheads had no mutagenic activity in this test system. (Reviewer's note: Due to toxicity, tests were performed over a low dose range; 3 of 4 doses were non-toxic and showed sufficient growth to evaluate mutagenicity. Testing at any lower doses was impractical).
Conclusions (contractor)	Rerun Tower Overheads did not induce an increase in revertant colonies in any Salmonella strain, tested at any dose level with or without metabolic activation in this single Ames test.
Data Quality *Reliabilities*	**1.** Reliable without restriction
Reference	Blackburn, G.R. 1981. An Ames Salmonella/mammalian microsome mutagenesis assay for the determination of potential mutagenicity of Rerun Tower Overheads from an olefins/aromatics plant. Study No. 1781-80. Mobil Environmental and Health Sciences Laboratory, Princeton, NJ. Ames B. N. et al. 1975. Mutat. Res. 31: 347-364.
Other *Last changed*	10/02/2001 (Prepared by a contractor for the Olefins Panel)

Robust Summary - Group 5: High Benzene Naphthas

Genetic Toxicity - in Vitro

Test Substance	**Rerun Tower Overheads** from Olefins/Aromatics Plant (light thermal cracked naphtha) CAS # 64741-74-8. Straw colored liquid; 40% benzene, 26% C5, 13% toluene, 20% other. Test substance is described as a sample of a Pyrolysis Gasoline distillate fraction and is similar to Pyrolysis gasoline, a stream included in the test plan.
Test substance	
Method	
Method/guideline followed	None specified. Standard method based on Slater et al., 1971, Green and Muriel, 1976, and Ames et al., 1973.
Type	Bacterial DNA repair
System of testing	Escherichia coil, Salmonella typhimurium
GLP	Not specified
Year	1978
Species/Strain	*E. coli* WP2 uvrA^{+} recA^{+}, WP100 uvrA^{-} recA^{-}; *S. typh*. TA1978 uvrB^{+}, TA1538 uvrB^{-}
Metabolic activation	Yes
Species and cell type	Sprague Dawley male rat liver (S9 fraction)
Quantity	50µl S9 fraction in 1.0ml S9 mix/plate
Induced or not induced	Aroclor 1254 induced (single ip injection of 500mg/kg, 5 days prior to sacrifice)
Concentrations tested	Spot test: 10µl/plate undiluted
Statistical Methods	None. Compounds that cause damage to DNA will more severely affect repair deficient strains than repair proficient stains. Toxic compounds that do not affect DNA will not induce differential toxicity.
Remarks for Test Conditions	Tester strains were stored in liquid nitrogen and fresh cultures were inoculated directly from frozen stock, grown overnight at 37^{0}C, re-diluted and grown to final cell concentration of 2x10^{8} cells/ml. Each test article-strain combination was plated in triplicate with and without metabolic activation. Log phase cultures (0.1ml) added to 2.5ml top agar were poured on Vogel-Bonner minimal medium plates. For plates without activation, a 6.5mm paper disc (antibiotic type) was placed in the center of each plate; 10µl test article is placed on disc. For plates with S9 activation, after top agar sets, a 9.5mm diameter hole was cut in agar in the center of the plate, the well was sealed with 0.1ml top agar, and 150µl of S9 mix/control or test article mix (14:1) added to the well. All inverted plates were incubated at 37^{0}C for 24hr. The diameter of any resulting zone of inhibition was measured in mm. Zone diameter of a repair deficient strain was divided by the zone diameter of the repair proficient parent strain. Positive control compounds were 4-nitro-quinoline-1-oxide (4-NQO; 30µg/plate) –S9, 2-aminofluorene (2-AF; 250µg/plate) +S9, and negative control was 25µg/plate penicillin. Tests were performed twice ± S9.
Results	
Genotoxic effects	In duplicate tests, average inhibition ratios induced by Rerun tower overheads –S9 were 1.4, 1.8 for *E. coli* WP100/WP2, and 1.3, 1.5 for *S. typh*. TA1538/TA1978 compared to negative control values of 1.0, 1.1, and 1.1, 1.2 in *E coli* strains and *S. typh*. strains, respectively, suggesting a weak differential killing of repair deficient strains without metabolic activation. Positive control ratios for 4-NQ –S9 were 2.3, 2.5 for *E coli* WP100/WP2, and 1.7, 1.6 for *S. typh*. TA1538/TA1978. In tests with metabolic activation (+S9), average inhibition ratios were 1.0, 1.0 for *E.coli* strains and 1.0, 1.0 for *S. typh*. strains in duplicate tests compared to negative control values of 1.1, 1.1, and 1.1, 1.1 in *E. coli* and *S. typh*. strains, respectively, indicating no test article induced toxicity. Positive control, 2-AF, inhibition ratios were 2.1, 2.1 for *E. coli* WP100/WP2, and 1.9, 1.4 for *S. typh*. TA1538/TA1978.

Conclusions (contractor)	Rerun tower overheads did cause weak differential killing in DNA repair deficient strains, *E. coli* WP100 and *S. typhimurium*. TA1538 in the absence of metabolic activation, suggesting that the test article can cause direct acting damage to bacterial DNA. No differential killing was observed in the presence of metabolic activation.	
Data Quality *Reliabilities*	**1.** Reliable without restriction	
Reference	Haworth, S.R. 1978. Bacterial DNA repair assay of Mobil Chemical Company Compound MCTR-125-78 (MRI #110). E. G. and G. Mason Research Institute, Rockville, MD. for Mobil Chemical Co, Edison, NJ Slater, E.E. et al. 1971. Cancer Res. 31: 970-973. Green, M.H.L. and Muriel, W.J. 1976. Mutat. Res. 38:3-32 Ames, B.N. et al. 1973. Proc. Natl. Acad. Sci., USA 70: 782-786.	
Other *Last changed*	2/28/2002 (Prepared by a contractor to the Olefins Panel)	

Robust Summary: High Benzene Naphthas

Genetic Toxicity - in Vitro

Test Substance	**Rerun Tower Overheads** from Olefins/Aromatics Plant (light thermal cracked naphtha) CAS # 64741-74-8. Straw colored liquid; 40% benzene, 26% C5, 13% toluene, 20% other. Test substance is described as a sample of a Pyrolysis Gasoline distillate fraction and is similar to Pyrolysis gasoline, a stream included in the test plan.
Test substance	
Method	
Method/guideline followed	Standard method, no guideline specified
Type	Cell transformation
System of testing	Mouse embryo cells
GLP	Yes
Year	1981
Species/Strain	BALB-c/3T3 mouse cell line
Metabolic activation	No
Species and cell type	NA
Quantity	NA
Induced or not induced	NA
Concentrations tested	Initial cytotoxicity: 0, 0.01, 0.1, 1.0, 10.0, 100.0µg/ml medium; Transformation: 0. 0.8, 4.0, 20.0 and 100µg/ml, diluted in dimethyl sulfoxide. Negative control was DMSO at 2.5% vol. concentration.
Statistical Method	T-test specified. Standard criteria for positive response is a two fold increase in type III foci at highest dose over vehicle control with or without a dose related response or a 2 fold increase at 2 or more consecutive doses.
Remarks for Test Conditions	Routine procedures were referred to Appendix 1 Standard Operating Procedures, which was not included with this report. Only specifics unique to this assay are presented. Due to the volatile nature of test material, the cytotoxicity assay and transformation assays were conducted in tightly capped T-25 flasks in sealed plastic bags. The pH of medium during the 72hr exposure period was maintained at 7.4 by 0.02M Hepes buffer in flasks. RTO was prepared as a 1% stock solution in DMSO, which, when added to culture medium at a 2.5% vol. conc. was a suspension. Despite limited solubility, RTO produced a dose-dependent cytotoxic effect after a 3-day exposure period. In the initial toxicity assay, RTO was added to flasks, seeded with BALB-c/3T3 cells, at concentrations of 0, 0.01, 0.1, 1.0, 10.0 and 100.0µg/ml, incubated for 3 days at 37^0C in a CO_2 in air incubator, after which cells were counted for survival. In the transformation assay, RTO was tested at 0, 0.8, 4.0, 20.0 and 100µg/ml. In a standard BALB-c/3T3 transformation assay, colony formation cultures (approx. 100 cells/culture) and transformation cultures (approx. 10^4 cells/culture, 20 cultures/dose) were seeded on day 1, exposed to test material for 2-3 days, and culture medium was changed on day 4. For transformation cultures, medium continued to be changed weekly to day 29. Colony formation cultures were fixed, stained and counted visually on day 8 to determine cloning efficiency; transformation cultures were fixed and stained on day 29 for focus counting and evaluation. Transformation frequency = total type III foci ÷ total cultures/dose. Positive control compound was 3-methyl cholanthrene (2µg/ml).
Results	
Genotoxic effects	RTO induced toxicity in BALB-c/3T3 cells after 3 days exposure at concentrations of 10µg/ml (59% viability) and at 100µg/ml (18% viability). In the transformation assay, inhibition of cloning efficiency (CE, clones/100 cells) occurred at 4.0µg/ml (89% CE), 20.0µg/ml (81% CE) and 100µg/ml (65% C.E.); cell toxicity was

	somewhat less than in the initial cytotoxicity assay [40% viability at 100µg/ml]. RTO did not induce statistically significant increased incidence of transformed foci compared to negative controls at any dose level. Values were 0.10 foci/flask, 2/20 flasks with foci at 100µg/ml, 0.0 foci/flask, 0/20 flasks with foci at 20.0µg/ml, 0.15 foci/flask, 3/20 flasks with foci at 4.0µg/ml, 0.10 foci /flask, 2/20 flasks with foci at 0.8µg/ml compared to 0.05 foci/flask, 1/20 flasks with foci in negative control group. [Reviewer's note: Negative control value of 1 focus/20 flasks was lower than control values in other concurrent studies on 2 other compounds in this series where negative controls had 4 foci in 20 flasks (0.20 foci/flask)]. Positive control compound, 3 methyl cholanthrene, induced 56 foci/19 flasks (2.95 foci/flask), 18/19 flasks with foci.
Conclusions (contractor)	Rerun tower overheads did not induce neoplastic transformation in BALB-c/3T3 cells and was not active in this test system.
Data Quality *Reliabilities*	**2**. Reliable with restrictions. Complete details of assay methods are not included in the report. Specifics of statistics are not supplied.
Reference	Tu, A.S. and Sivak, A. 1981. BALB-c/3T3 Neoplastic transformation assay on 0818802, 08188003 and 08188005 (Rerun tower overheads). ALD Ref. #86374. Arthur D. Little, Inc. Cambridge, MA for Mobil Oil Corp, Study #1771-80, Princeton, NJ Roy, T.A., 1981. Analysis of rerun tower bottom oil by combined capillary gas chromatography/mass spectrometry. Study #1272-81-. Toxicology division, Mobil Oil Co., Princeton, NJ
Other *Last changed*	12/07/01 (Prepared by a contractor to the Olefins Panel)

Robust Summary: High Benzene Naphthas

Genetic Toxicity - in Vitro

Test Substance	**Rerun Tower Overheads** from Olefins/Aromatics Plant (light thermal cracked naphtha) CAS # 64741-74-8. Straw colored liquid; 40% benzene, 26% C5, 13% toluene, 20% other. Test substance is described as a sample of a Pyrolysis Gasoline distillate fraction and is similar to Pyrolysis gasoline, a stream included in the test plan.
Test substance	
Method	
Method/guideline followed	None specified. Standard method based on Clive and Spector, 1975
Type	Mammalian cell mutation assay
System of testing	Mouse lymphoma cells
GLP	Not specified
Year	1979
Species/Strain	Mouse lymphoma L5178Y TK+/- cells
Metabolic activation	Yes
Species and cell type	Sprague Dawley males rat liver (S9 fraction)
Quantity	50µl S9 fraction/ml S9mix)
Induced or not induced	Aroclor 1254 induced (single ip injection of 500mg/kg, 5 days prior to sacrifice)
Concentrations tested	-S9 cloned doses: 0.0, 0.013, 0.018, 0.024, 0.032, 0.042, 0.056, 0.075, and 0.10µl/ml +S9 cloned doses: 0.0, 0.048, 0.063, 0.085, 0. 11, 0.15, 0.20, 0.27, and 0.36µl/ml. All doses diluted in acetone
Statistical Methods	None. Compound was designated as mutagenic if it induced a mutation frequency (mutant cells/10^4 surviving cells) greater than 3 times the standard error (S.E. [f]) calculated by formula from the viable counts and total mutant cells (trifluorothymidine resistant cells) at each dose level.
Remarks for Test Conditions	Freshly prepared actively growing cultures of L5178Y cells ($1x10^6$ cells/ml) were dispensed in 6ml aliquots into 44 polypropylene centrifuge tubes. Rerun tower overheads, solubilized in acetone, beginning at a concentration equal to LD90 from a preliminary toxicity test, was diluted over 15 serial 1/8 log dilutions, producing 16 dose levels decreasing approximately 100 fold from highest to lowest, and added to cells in the centrifuge tubes. Four ml of S9 activation mixture or 4ml culture medium was added, yielding a final cell suspension of $0.6x10^6$ cells/ml. Positive control compounds were ethyl methyl sulfonate (EMS, 1.0µl/ml) –S9 and 7,12-dimethylbenzanthracene (7,12-DMBA, 2.5µl/ml) +S9 cultures. All tubes were gassed with 5% CO2/air and placed on a roller drum for 4hrs at 37^0C in the dark. At the end of exposure, calls were washed with fresh medium, re-suspended, gassed, replaced on roller drum at 37^0C and incubated for 3 days with a cell population adjustment every 24 hrs to maintain a cell population density of $0.3x10^6$ cells/ml. After 3 days expression, 8 cultures ± S9, which exhibited toxicity from 10-90% growth inhibition during the expression period, were selected for cloning. At cloning, cells were placed in restrictive suspension medium containing trifluorothymidine (TFT, 1µg/ml) that allows only TK-/- cells to grow. Two Florence flasks/concentration ± S9, one for restrictive medium, on for viable cell counts, were filled with 100ml cloning medium and maintained at 37^0C. Six 100mm petri plates/concentration ± S9 were prepared, 3 for restrictive medium, 3 for viable cell counts. Cell counts were made from each centrifuge tube to determine the volume of cell population = $3x10^6$cells. This volume was retained, centrifuged and the supernatant discarded except for 2ml in which cells were re-suspended and placed in restrictive medium flask. A $5x10^{-4}$ dilution was prepared and added to the appropriate viable count flask containing 100ml cloning medium. After this dilution, 1 ml of TFT stock solution was added to the restrictive medium flask and incubated

	with shaking (125rpm) at 37^{0}C for 15min. Flasks were removed, 33ml of cell suspension was pipetted into each of 3 appropriately labeled plates and placed in the cold (4^{0}C) for 20 min to accelerate gelling. Plates were removed and incubated at 37^{0}C in humidified 5% CO2/air for 10 days. At the end of incubation, plates were scored for total number of colonies/plate, 3 counts/plate, on an automated colony counter. Mutation frequency (MF) = avg. number of colonies in 3 restrictive medium plates ÷ avg. number of colonies x10^4 in 3 corresponding viable count plates. Induced mutation frequency (IMF) = MF test article – MF solvent control.
Results Genotoxic effects	In cultures without metabolic activation, the two highest concentrations cloned, 0.10µl/ml (MF=1.4, IMF=0.8) and 0.075µl/ml (MF=1.0, IMF=0.4) exhibited slight dose related increases in IMF compared with acetone control (MF=0.6); only the 0.10µl/ml concentration caused a doubling of MF over controls. EMS positive control values were MF=27.1, IMF=26. The first activated assay was discarded due to loss of positive control cultures by contamination. In the repeat test with metabolic activation, 2 dose concentrations had MF 2 times greater than acetone controls: the highest dose cloned, 0.36µl/ml (MF=0.8, IMF=0.4) and 0.15µl/ml, the 4th highest dose cloned (MF=0.9, IMF=0.5) versus control (MF=0.4). However, intervening cloned doses of 0.20, and 0.27µl/ml did not show increased MF; the values for the positive doses were not dose related and were within the range of experimental error for the assay. Positive control values +S9 for 7,12- DMBA were MF=2.6, IMF=2.0.
Conclusions (contractor)	Without metabolic activation, Rerun tower overheads appears to induce a weak mutagenic response at the two highest doses only; a dose response trend was not observed in the 6 lower doses cloned. Test article did not induce significant mutagenic activity in cultures containing S9, suggesting that any mutagenic activity is suppressed or inactivated by the presence of the liver microsome metabolizing system.
Data Quality *Reliabilities*	**1.** Reliable without restriction.
Reference	Kirby, P.E. et al., 1979. An evaluation of mutagenic potential of MCTR-125-78 (MRI #110) employing the L5178Y TK+/- mouse lymphoma assay. E.G. and G. Mason Research Institute, Rockville, MD for Mobil Chemical Co., Edison, NJ Clive, D., and Spector, J.F.S. 1975. Mutat. Res. 31: 17-29
Other *Last changed*	2/28/2002 (Prepared by a contractor to the Olefins Panel)

Robust Summary: High Benzene Naphthas

Genetic Toxicity - in Vitro

Test Substance	
Test substance	**Rerun Tower Overheads** from Olefins/Aromatics Plant (light thermal cracked naphtha) CAS # 64741-74-8. Straw colored liquid; 40% benzene, 26% C5, 13% toluene, 20% other. Test substance is described as a sample of a Pyrolysis Gasoline distillate fraction and is similar to Pyrolysis gasoline, a stream included in the test plan.
Method	
Method/guideline followed	None specified. Standard method based on Bertram, 1977
Type	Mammalian cell transformation assay
System of testing	Mouse C3H embryo cells
GLP	Not specified
Year	1978
Species/Strain	Mouse embryo cells/ C3H 10T½
Metabolic activation	No
Species and cell type	NA
Quantity	NA
Induced or not induced	NA
Concentrations tested	0, 0.625, 1.25, 2.5 and 5.0µl/ml, all diluted in acetone
Statistical Methods	None. A positive response is determined by the appearance of any type II foci (50% can be malignantly transformed) and type III foci (85% can be malignantly transformed) compared to negative controls. The C3H 10T½ cell line has no spontaneous transformation.
Remarks for Test Conditions	For the preliminary toxicity assay, cells (200/plate) were exposed to Rerun tower overheads diluted in acetone, over a range of concentrations from 0.0003-5.0µl/ml, at 2-fold dilutions for 18hrs; cells were then washed, re-fed with fresh Eagle's basal medium and incubated for 10 days in 5% CO2/air at 37^0C. After incubation, cells were washed, fixed with absolute methanol (20 min) and stained with Giemsa (30 min); number of cells/plate were counted and cloning efficiency (CE) determined=Avg. number colonies/plate ÷ number cells plated x100. In the transformation assay, cells in late log phase were plated at a concentration of $1x10^3$ cells/60mm petri dish. Cultures for concurrent toxicity determination were prepared at 200 cells/plate. After 24 hrs, cultures were treated with appropriate test article concentrations in 25µl volumes at 4 dose levels, 12 plates/dose, in decreasing 2-fold dilutions from concentrations which exhibit 25-75% relative CE. Positive control compound was 7, 12-dimethylbenzanthracene (7, 12-DMBA, 0.5µg/ml). After 18hr treatment, test article was removed, cultures were re-fed, and re-incubated. Toxicity plates were incubated for 10 days, stained and CE determined. Transformation cultures were re-fed weekly until 35 days after removal of test article had elapsed. All plate cultures were washed, fixed, stained and scored for the presence of type II and type III foci by macroscopic and microscopic examination. Type II foci show massive piling up in virtually opaque monolayers, cells are moderately polar. Type III foci are composed of highly polar, fibroblastic, multilayered, criss-crossed arrays of densely stained cells.
Results	
Genotoxic effects	Rerun tower overheads induced 71% relative cloning efficiency at 5.0µl/ml; transformation assay was performed at 2-fold dilutions from 5.0µl/ml. In the toxicity study conducted in parallel with the transformation assay, test article induced 100% cell death at 5.0µl/ml. In the transformation assay, sufficient cells survived to form a confluent layer in 8/12 plates at 5.0µl/ml dose level after 35 days. No indication of type II or type III foci were induced by rerun tower overheads at any dose level. Positive control, 7,12-DMBA induced 9 type II and

	12 type III foci on 12 plates.
Conclusions (contractor)	Rerun tower overheads does not induce cell transformation in mouse embryo C3H 10T½ cells.
Data Quality *Reliabilities*	**1.** Reliable without restriction
Reference	Jensen, E.M., and Thilager, A.K. 1978. C3H 10T½ cell transformation assay, Mobil Chemical Co. Compound MCTR-125-78 (MRI #110). E.G. and G. Mason Research Institute, Rockville, MD Bertram, J.S. 1977. Cancer Res. 37: 514-523
Other *Last changed*	2/28/2002 (Prepared by a contractor to the Olefins Panel)

Robust Summary - Group 5: High Benzene Naphthas

Genetic Toxicity - in Vivo

Test Substance	
Remarks	**Rerun Tower Overheads** from Olefins/Aromatics Plant (light thermal cracked naphtha) CAS # 64741-74-8. Straw colored liquid; 40% benzene, 26% C5, 13% toluene, 20% other. Test substance is described as a sample of a Pyrolysis Gasoline distillate fraction and is similar to Pyrolysis gasoline, a stream included in the test plan.
Method	
Method/guideline followed	None specified. Standard method based on Bowman, 1969; Lewis, 1954; Mendelson, 1976
Type	*Drosophila* assays for point mutation, chromosome aberrations & chromosome loss
GLP	Not specified
Year	1979
Species	Drosophila melanogaster
Strain	Dominant lethal: Canton S; Y chromosome loss: males red/white eye; females white/white eye; Somatic reversion: males white ivory ($\underline{w^i}$), yellow body ($\underline{y}$), echinus ($\underline{ec}$); females $\underline{w^i}/\underline{w^i}$; Bithrox test: males Ultrabithorax ($\underline{Ubx}$); females bithorax ($\underline{bx^{34e}}$); Sex-linked recessive lethal: males Canton S; females $\underline{Basc}/\underline{Basc}$
Sex	Males and females
Route of administration	Aerosol
Doses/concentration levels	0.3ml in 50ml air
Exposure period	10 min.
Statistical methods	Events in these tests have very low probabilities. Analysis based on Poisson distribution with fiducial limits computed according to Stevens, 1942.
Remarks for Test Conditions.	*Drosophila* stocks were maintained in agar/corn meal/sugar/yeast medium at 23^0C. One set of stocks was transferred each week to isolate virgin females for breeding. Four days are required for maturation of *Drosophila* sperm cells after meiosis. In all assays, treated males were mated for 3 days only to assure use of a uniform sample of treated sperm. In all assays, test article was administered as an aerosol, 0.3ml in 50ml volume of air.when administered for 1hr anesthesized flies and killed approximately 30%. Longer treatments reduced fertility. Exposure in all assays was 10 minutes in duration. Somatic reversion of white-ivory: Larvae from mating of males carrying 5 copies of white-ivory gene on the X chromosome ($\underline{w^i}$, $\underline{y}$, $\underline{ec}$) with $\underline{w^i}/\underline{w^i}$ females were treated with aerosolized test article for 10 min. Positive control compound was 0.04M mitomycin C. Larvae were washed and transferred to culture bottles to complete development. After eclosion, female offspring, genotype Qn(1)$\underline{w^i}$, $\underline{y}$, $\underline{ec}/\underline{w^i}$ were scored for red spots in the eye, which signals reversion of $\underline{w^i}$ to a pigment cell. Y chromosome loss: Males carrying a duplication of the gene for normal (red) eyes on Y chromosome and a mutant allele, white ($\underline{w}$) on the X chromosome were treated with aerosolized test article for 10 min and mated to white-eyed females ($\underline{w}/\underline{w}$). Positive control were males exposed to 3kr X-rays. Frequency of occurrence of white-eyed male progeny measured frequency of Y chromosome loss. Dominant lethal mutations: Defined as any genetic change that blocks development prior to hatching. Treated Canton S males were mated with untreated females in nylon net cages on Welch's grape juice solidified with 2% agar. After 12 hr, agar plates were removed and stored at room temp. (23^0C) for 30 hrs. Positive control was 0.04M ethyl methane sulfonate. Eggs were scored for hatching after 30hrs.

	Bithorax test of Lewis: Occurrence of rearrangements with one breakpoint between centromere and the locus of bithorax (bx) was determined by scoring offspring of treated Ultrabithorax males and bithorax females. Males treated with 3kr X-rays were the positive controls. Distinctive phenotype was the presence of a mesonotum Sex-linked recessive lethals: Canton-S males, treated with test article, were mated with Basc (balancer X chromosome) females. Individual (F1) female progeny were mated with Basc males. Any single female culture containing at least 20 flies (F2), at least 8 of which are males, but no males are wild type, is scored as a lethal. Ethyl methane sulfonate (0.04M) treated males were the positive controls. A repeat study was performed due to loss of cultures to dessication.
Results Genotoxic effects NOAEL (NOEL) LOAEL (LOEL)	Rerun tower overheads did not induce genetic damage in *Drosophila melanogaster* under experimental conditions in any test employed. The repeated sex-linked recessive lethal test, performed due to technical problems in the initial assay, did not demonstrate any genetic damage in *Drosophila* from exposure to the test article
Conclusions (study authors)	Rerun tower overheads did not induce genetic damage in *Drosophila melanogaster*.
Data Quality *Reliabilities*	**1.** Reliable without restrictions.
References	Bowman, J.T. 1979. *Drosophila* mutagenicity assays of Mobil Chemical Compound MCTR-125-78. MRI #110. E.G. and G. Mason Research Institute, Rockville, MD, for Mobil Chemical Co., Edison, NJ. Bowman, J.T. 1969. Mutat. Res. 7: 409-415 Lewis, E.B. 1954. Am. Nat. 88: 225-239 Mendelson, D. 1976. Mutat. Res. 41: 269-276 Stevens, W.L. 1942. J. Genetics 43: 301-307
Other *Last changed*	2/28/2002 (Prepared by a contractor to the Olefins Panel)

Robust Summary: High Benzene Naphthas

Repeated Dose Toxicity

Test Substance	**Rerun Tower Overheads** from Olefins/Aromatics Plant (light thermal cracked naphtha) CAS # 64741-74-8. Straw colored liquid; 40% benzene, 26% C5, 13% toluene, 20% other. Test substance is described as a sample of a Pyrolysis Gasoline distillate fraction and is similar to Pyrolysis gasoline, a stream included in the test plan.
Remarks	
Method	
Method/guideline followed	None specified, comparable to standard methods
Test type	Subacute
GLP	Not specified
Year	1980
Species	Rabbit (4/sex/group)
Strain	New Zealand White
Route of administration	Dermal
Duration of test	21 days
Doses/concentration levels	0, 0.1, 0.5, and 1.0ml/kg/day
Sex	Male and females
Exposure period	Continuous (no wipe-off)
Frequency of treatment	Once/day
Control group and treatment	Males and females (4M, 4F), saline (0.9%), 1ml/kg/day
Post exposure observation period	3 days
Statistical methods	Bartletts test, analysis of variance, Scheffe's multiple pair wise comparison, Gaines and Howell's multiple pair wise comparison
Test Conditions	Rabbits were housed individually in stainless steel cages and received water and rabbit chow diet, ad lib. Initial body wt ranged from 2455-3005g for males and 2455-3035g for females. Four rabbits of each sex were assigned to treatment groups of 0, 0.1, 0.5, and 1.0ml of neat test article/kg/day. Control rabbits received 1.0ml/kg/day of 0.9%NaCl. Prior to initiation, the dorsal dosing area was clipped free of hair and clipping was done periodically during the study. The exposure area was abraded with minor incisions deep enough to penetrate the stratum corneum but not deep enough to produce bleeding. Abrasions were made prior to the first application, and thereafter, on the first day of each week. Test article was applied to the skin once a day, starting on day 1, for 21 consecutive days; rabbits were sacrificed between day 22 and day 24. Each rabbit wore a plexiglass collar for the entire study to retard ingestion of test article. Rabbits were observed daily for mortality and moribundity, food/water intake, general appearance/behavior, toxic/pharmacological effects, and dermal reactions for 24 consecutive days. Dermal irritation was graded each morning prior to dosing. Food consumption was determined 3 times /wk and body weight on days1, 8, 15, and at termination. Prior to study initiation and during wk 3, hematocrit (Hct), hemoglobin (Hgb), erythrocyte count (RBC), total leukocyte count (WBC) and differential leukocyte count, mean cell volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin conc. (MCHC), serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), alkaline phosphatase (Alk Phos), fasting glucose, and blood urea nitrogen (BUN); urine (pH, specific gravity, glucose, ketones, total protein, bilirubin[BIH]), and microscopic examination of sediment were evaluated. Rabbits were sacrificed on day 24; necropsies were performed and gross observations recorded for all rabbits. Liver, kidney, thyroid, and adrenals were weighed and preserved for microscopic analysis along with brain, pituitary, lung, heart, spleen, pancreas, urinary bladder, testis/ovary, skin, and any unusual lesions.

Results	
NOAEL (NOEL)	NOAEL <0.10ml/kg/day both sexes (skin irr). LOAEL = 0.1ml/kg/day both sexes (skin irr)
LOAEL (LOEL)	
Remarks	NOAEL = 1.0ml/kg/day both sexes (systemic effects). LOAEL >1.0ml/kg/day both sexes (systemic effects). Two rabbits died during the study from cardiac puncture blood sampling. No test article induced effects were noted during clinical observations. Two 0.1ml/kg/day group males and one female showed erythema from day 10 to termination; 3 0.5ml/kg/day group males showed erythema from day 8 to termination; all 0.5ml/kg/day males and females, and 1.0ml/kg/day males and females had well defined erythema from day 9 to termination. Edema was not present in any rabbits. Skin thickening was noted in all test article groups from wk 1 to termination. Fissuring was seen in 3 0.1ml/kg/day males, 3 0.5ml/kg/day males and all 1.0ml/kg/day males; all test article treated females showed fissuring. Necrosis was present in 2males and 3 females given 0.1ml/kg/day, 3males and all females given 0.5ml/kg/day, and all males and females given 1.0ml/kg/day. There were no significant changes in body wt or food consumption between controls and treatment groups. Terminal basophilic values were elevated in all male test article treated groups; all other hematology values were comparable to controls. Urinalysis findings were unremarkable. There were no significant differences in organ wt between control and any treatment group. Histological evaluation for the skin showed effects consistent with gross observations with no dose-related gradation of severity between doses, including hyperkeratosis, acanthosis, accumulation of heterophils, and cellular debris in stratum corneum, and hyperplasia of sebaceous glands. There were no abnormal microscopic findings attributable to test article administration in organs from the three treatment levels compared to controls.
Conclusions (study authors)	Daily epidermal application of test article resulted in skin irritation at the application site.
Quality Reliabilities	**2.** Reliable with restriction. There was no mention of GLP.
References	Fieser, S., Alsaker, R.D., Brown, H.R., and Wolfe, G.W. 1980. 21-Day dermal irritation study in rabbits. Proj. #230-213. Hazleton Laboratories America, Inc., Vienna, VA. For Mobil Chemical Co., Edison NJ (This study was actually for subacute toxicity, not only skin irritation)
Other Last changed	2/28/2002 (Prepared by a contractor to the Olefins Panel)

Robust Summary: High Benzene Naphthas

Developmental Toxicity/Teratogenicity

Test Substance	**Rerun Tower Overheads** from Olefins/Aromatics Plant (light thermal cracked naphtha) CAS # 64741-74-8. Straw colored liquid; 40% benzene, 26% C5, 13% toluene, 20% other. Test substance is described as a sample of a Pyrolysis Gasoline distillate fraction and is similar to Pyrolysis gasoline, a stream included in the test plan.
Remarks	
Method	
Method/guideline followed	None specified, conforms to standard method
Test type	Teratology
GLP	Yes
Year	1981
Species	Rabbit
Strain	New Zealand White
Route of administration	Oral gavage
Concentration levels	0, 10, 25, and 50mg/kg/day, diluted in corn oil
Sex	Pregnant females (16/group)
Exposure period	Day 6-28 of gestation
Frequency of treatment	Once/day
Control group and treatment	16 pregnant females received 0.5ml/kg/day corn oil
Duration of test	29 days
Statistical methods	Chi square with Yates' correction for 2x2 contingency table and /or Fisher's exact probability test; Mann-Whitney U test; analysis of variance (one-way), Bartlett's test and t-test using Dunnett's multiple comparison tables. Level of significance $p<0.05$.
Remarks for Test Conditions.	In an initial study, RTO was administered by oral gavage, undiluted to 16 pregnant rabbits/group at levels of 0 (distilled water), 10, 25 and 50 mg/kg/day. Forty-two rabbits died: 14, 11, 13, and 13 in the 0, 10, 25 and 50mg/kg/day groups respectively. Due to excess mortality in all treated groups and the controls, the study was terminated and repeated at the same concentrations diluted in corn oil. Sixty-four sexually mature virgin female rabbits (7 months old, 3.46-4.19kg at study initiation) were acclimated for 59 days, assigned a unique animal number and ear-tagged when placed on study. All rabbits were individually housed in suspended wire cages and maintained in a temperature, humidity, and light (12 hr light/dark cycle) controlled environment. Certified rabbit chow and tap water were available ad lib. Only coccidiosis-free rabbits were used in the study. Prior to insemination, females were randomly assigned to groups (16/group) according to body wt, by a computer-generated program. Sperm was collected from each of 6 proven breeder males of the same source and strain, using an artificial vagina. Semen was immediately evaluated for motility, and was used for insemination only if motility was≥50%. Useable ejaculate was diluted in 0.9%NaCl at 35^0C; 0.25-0.50ml of dilute semen was introduced into the anterior vagina. Ovulation was induced by injection of 100 units chorionic gonadotropin (Ayerst, NY) in the marginal ear vein of the female immediately after insemination. Semen from one male was used to inseminate an equal number of females in each group. Inseminations were performed on two consecutive days; an equal number of females was inseminated in each group/day, designated as day 0 of gestation. RTO was mixed with corn oil daily at appropriate doses and shaken by hand. No analysis of dosing solution was reported. Negative control dams were given 0.5ml corn oil/kg/day, the volume equal to the highest treatment group. Individual doses were determined from individual body wt on day 6 of gestation. Females

	were observed daily for mortality, overt changes in appearance and behavior, and, from day 6-29 of gestation, for clinical signs of toxicity. One dam aborted on gest. day 19 and remained on study until scheduled sacrifice; aborted material was discarded. Body wt was recorded on gestation days 0, 6, 12, 18, 24, and 29. On gest. day 29, all females were sacrificed by overdose of sodium pentabarbitol, uteri were excised and weighed prior to removal of fetuses. Number and location of viable and non-viable fetuses, early and late resorptions, number of total implantations, and corpora lutea were recorded. Abdominal and thoracic cavity and organs of dams were examined grossly and discarded. Uteri from apparently non-gravid animals were opened and placed in 10% ammonium sulfide solution to confirm pregnancy status. All fetuses were individually weighed and examined for external malformations and variations. Each fetus was internally sexed and examined for internal malformations and variations, including the brain by mid-coronal slice. The heart was dissected using Staples' technique. Eviscerated, skinned fetuses were individually numbered and tagged, fixed in alcohol, macerated and stained with Alizarin Red S for skeletal examination. Fetal findings were classified as malformations or genetic or developmental variations.
Results	
NOAEL maternal toxicity	NOAEL maternal = 25mg/kg/day (based on 1 abortion at 50mg/kg/day)
NOAEL developmental toxicity	NOAEL developmental = 50mg/kg/day; both values assigned by reviewer
Maternal effects	Maternal survival was 100% in all groups. Slight increase in matted haircoat (primarily in nasal region) and slight reduction in fecal material beneath cages was noted in 50mg/kg/day rabbits. Occasional instances of nasal discharge, soft stool, hair loss and scabbing were noted in all groups during gestation. One 50mg/kg/day rabbit aborted on day 19 of gestation. Maternal body wt in treated rabbits at all doses were comparable to controls throughout treatment (gest. day 6-28) and gestation (day 0-29) periods. Mean maternal adjusted body wt (minus gravid uterus) at termination in all groups was comparable to controls. Pregnancy ratio was 87.5, 81.3, 81.3, 93.8 in 0, 10, 25 and 50mg/kg/day groups, respectively. Two control dams and one 50mg/kg/day dam had all resorptions. There were no biologically or statistically significant differences in mean number of corpora lutea, total implantations, early or late resorptions, postimplantation loss, viable fetuses, fetal sex index, or mean fetal body wt in any RTO treated group compared to controls.
Embryo/fetal effects	Average litter size was 6.1, 6.5, 6.4, and 5.9 and average fetal body wt (both sexes) was 38.9, 43.0, 42.5, and 42.4g in 0, 10, 25, and 50mg/kg/day groups, respectively. There were no biologically or statistically significant differences in number of litters with malformations (external, soft tissue, skeletal) in any treated group compared to controls: 5/12 litters (85 pups), 1/13 litters (84 pups), 3/13 litters (83 pups) and 5/13 litters (82 pups examined) in 0, 10, 25, and 50mg/kg/day, respectively. In the 50mg/kg/day group, one occurrence of atlas-occipital anomaly and one occurrence of enlarged heart with great vessel anomaly, were observed in 2 separate litters. Scoliosis was present in all groups including control, with slightly higher incidence in the 50mg/kg/day group., but incidences were within the range of historical control data for this laboratory. Fetuses and litters with genetic or developmental variations were comparable in all groups.
Conclusions (study authors)	Rerun tower overhead did not produce a teratogenic response in pregnant New Zealand White rabbits when administered orally in corn oil vehicle at dose levels of 10, 25 and 50mg/kg/day. With the exception of one 50mg/kg/day female that aborted, minimal maternal toxicity was observed at any dose level.

Data Quality *Reliabilities*	**2.** Reliable with restrictions. Analysis of test article concentration in corn oil vehicle was not performed.
References	Schardein, J.L. 1981. Teratology study in rabbits: Rerun tower overheads (MRTC-171-79) IRDC #450-011. International Research and Development Corp., Mattawan, MI. for Mobil Petrochemicals Division, Edison, NJ
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