REFINERY GASES CATEGORY ANALYSIS AND HAZARD CHARACTERIZATION

Submitted to the US EPA

by

The American Petroleum Institute (API)
Petroleum HPV Testing Group

www.petroleumhpv.org

Consortium Registration # 1100997

June 10, 2009

REFINERY GASES CATEGORY ANALYSIS AND HAZARD CHARACTERIZAION

Table of Contents

List of Tables

EXECUTIVE SUMMARY

General Description of the Refinery Gases Category

The 62 Refinery Gas substances in this test plan are primarily produced in petroleum refineries as the light end fractions of numerous distillation and cracking processes, or in gas plants that separate natural gas and natural gas liquids. All refinery gases in this category are comprised of predominantly one to four carbon atom hydrocarbons and inorganic components such as ammonia, hydrogen, nitrogen, hydrogen sulfide, mercaptans, carbon monoxide and carbon dioxide. Several refinery gases also contain benzene and/or 1,3-butadiene. These gases exist as substances in closed systems in the refinery, with none being sold as finished products because one or more constituents of refinery gases make them unsuitable for commercial sale. The refinery gases can be used within the refinery as fuel gases to provide energy for other refinery processes. They can also undergo further refining to separate components and make them into commercially viable products.

The Refinery Gases Category contains 62 refinery gases and 14 supplementary individual chemicals. The supplemental chemicals are included in this category to characterize the SIDS hazard endpoints for the refinery gases. The defining characteristics of Refinery Gases are (1) the presence of inorganic compounds which are the dominant hazard in the substance and (2) the fact that Refinery Gases are substances that are not sold on the open market in the US. Their physical and chemical characteristics require that they stay within rigorously contained systems within the manufacturing facility.

Refinery Gases Category Rationale

All Refinery Gases Category members contain one or more inorganic compounds in addition to hydrocarbons as listed in the stream TSCA definitions. The inorganic components of the Refinery Gases (with the exception of asphyxiant gases such as hydrogen and nitrogen) are typically more toxic than the C1 – C4 and C5 – C6 hydrocarbon components to both mammalian and aquatic organisms. Unlike other petroleum product categories (*e.g.* gasoline, diesel fuel, lubricating oils, etc.), the inorganic and hydrocarbon constituents of refinery gases can be evaluated for hazard individually to then predict the screening level hazard of the Refinery Gases Category members. The 12 refinery gas constituents identified to characterize refinery gas category member hazard are:

- Inorganic Gases
  - Ammonia
  - Carbon Monoxide
  - Ethyl mercaptan
  - Hydrogen sulfide
  - Methyl mercaptan
- Hydrocarbon Gases
  - Benzene
  - 1,3-Butadiene
  - C1 – C4 Hydrocarbons
  - C5 – C6 Hydrocarbons
- Asphyxiant Gases
  - Carbon dioxide
  - Hydrogen gas
  - Nitrogen gas

Physical-Chemical Properties and Environmental Fate

Refinery gases are mixtures of individual inorganic and organic compounds existing in the gaseous phase at normal environmental temperatures. These constituents typically have extremely low melting and boiling points. They also have high vapor pressures and low octanol/water partition coefficients. The aqueous solubility of these components varies, and can range from low parts per million (hydrogen gas) to several hundred thousand parts per million (ammonia). The environmental fate characteristics of refinery gases are governed by these physical-chemical

attributes. All components of these gases will partition to the air where interaction with hydroxyl radicals may be either an important fate process or have little influence, depending on the constituent. Many of the gases are chemically stable and may be lost to the atmosphere or simply become involved in the environmental recycling of their atoms. Some show substantial water solubility, but their volatility eventually causes these gases to enter the atmosphere.

Environmental Effects

Several of the inorganic constituents in refinery gases are highly hazardous to aquatic organisms as demonstrated in laboratory toxicity tests where exposure concentrations can be maintained over time. Hydrogen sulfide was the most toxic constituent to fish (LC50 ranged 0.007 to 0.2 mg/L) and invertebrates (EC50 ranged 0.022 to 1.07 mg/L). Acute toxicity data for ammonia also showed this to be a relatively toxic component, with several LC/EC50 values below 1 mg/L for fish and invertebrates (0.083 to 1.09 mg/L and 0.53 to 22.8 mg/L, respectively). The hydrocarbon components in refinery gases were generally less toxic. Acute LC/EC50 values for this constituent group ranged roughly from 1 to 100 mg/L. Although the LC/EC50 data for the individual gases illustrate the potential toxicity to aquatic organisms, aqueous concentrations from releases of these gases would likely not persist in the aquatic environment for a sufficient duration to elicit toxicity. Based on a simple conceptual exposure model analysis, emissions of refinery gases to the atmosphere would not likely result in acutely toxic concentrations in adjacent water bodies because such emissions will tend to remain in the atmosphere.

Human Health Effects

The screening level mammalian health hazards associated with Refinery Gases have been characterized by the constituents (as listed above) of each refinery gas. Refinery gas constituent hazard data were used to characterize SIDS endpoints for each of the 62 Refinery Gases in the category. To accomplish this, the endpoint value (acute LC_{50}, reproductive toxicity NOAEL/LOAEL, etc.) for a specific gas constituent has been adjusted for dilution of each constituent in the respective refinery gas. This adjustment for the dilution of each component in a refinery gas represents the calculated concentration of the refinery gas required to reach the toxicity value (LC_{50}, NOAEL, etc.) corresponding to the pure substance. For example, if the LC_{50} for neat (100%) hydrogen sulfide is 444 ppm, the LC_{50} for a refinery gas containing 20% (wt./v) hydrogen sulfide would be 2,220 ppm; *i.e.* it would take five times more of the refinery gas containing 20% hydrogen sulfide to produce the same effect as pure hydrogen sulfide, when the refinery gas is diluted with air. In many cases, there is more than one potentially toxic constituent in a refinery gas. In those cases, the constitutent that is most toxic for a particular endpoint in an individual refinery stream is used to characterize the endpoint hazard for that stream. A more detailed explanation with examples of these calculations, along with the calculations for each of the 62 refinery gases used to determine which constituent to use to characterize mammalian SIDS endpoint-specific hazard for each gas is presented in the body of the document.

This approach to correct for the concentration of the individual refinery gas constitutents to estimate the potential toxicity for mammalian endpoints makes it difficult to draw general conclusions as to which constituents are the most hazardous for human health effects of refinery gases as a category. The hazard potential for each mammalian endpoint for each of the 62 refinery gases is dependent upon each refinery gas constituent endpoint toxicity values (LC50, LOAEL, etc.) and the relative concentration of the constituent present in that gas. It should also be noted that for an individual refinery gas, the constituent characterizing toxicity may be different for different mammalian endpoints, again, being dependent upon the concentration of the different constituents in each, distinct refinery gas.

1. DESCRIPTION OF REFINERY GASES CATEGORY

Background
The original Petroleum Gases Category of 161 substances has been split into two separate categories; (1) the Petroleum Hydrocarbon Gases, and (2) the Refinery Gases. This Category Analysis Document provides the HPV hazard characterization for the Refinery Gases Category. This division of petroleum gases into two categories is more consistent with petroleum gas categories developed by CONCAWE (Conservation of Clean Air, Water in Europe; the European petroleum industry trade association) and used in European Union legislation.

General Description of the Refinery Gases Category
The Refinery Gases Category contains 76 chemical substances. Of these 76 substances, 62 are refinery gases and 14 are individual supplemental chemicals:

- Sixty-one substances are petroleum refinery gases listed on the 1990 HPV substances list;
- One substance is a refinery gas not listed on the 1990 HPV list; and
- Fourteen substances are included in the category as supplemental chemicals (nine inorganic chemicals and five hydrocarbons)

The supplemental chemicals are included in this category to characterize the SIDS endpoints for the refinery gases (as described below). These are included as single chemicals because they either exist in refinery gases at more than trace levels or are known to cause adverse effects in mammalian or aquatic organisms. A list of all category members by CASRN and their respective TSCA definition is provided in Appendix 1.

The 62 Refinery Gas substances in this test plan are primarily produced in petroleum refineries as the light end fractions of numerous distillation and cracking processes, or in gas plants that separate natural gas and natural gas liquids. These gases exist as substances in closed systems in the refinery, with none being sold as finished products because one or more constituents of refinery gases make them unsuitable for commercial sale. The refinery gases can be used within the refinery as fuel gases to provide energy for other refinery processes. They can also undergo further refining to isolate specific components for use as commercial products. All refinery gases in this category are comprised of predominantly one to four carbon atom hydrocarbons and contain other components such as ammonia, hydrogen, nitrogen, hydrogen sulfide, mercaptans, carbon monoxide, or carbon dioxide. Several refinery gases also contain benzene and/or butadiene. As with most of the substances handled within the petroleum industry, these gaseous substances are commonly referred to as "refinery streams."

The defining characteristics of Refinery Gases are (1) the presence of inorganic compounds which are the dominant hazard in the substance and (2) the fact that Refinery Gases are substances that are not sold on the open market in the US. Their physical and chemical characteristics require that they stay within rigorously contained systems. As mentioned, many Refinery Gases are burned within the refinery to power other refining operation processes. Additionally, they may be transferred by direct pipeline between neighboring refineries and petrochemical plants, within limited geographical distances (~ 30 miles or less). The potential for human and environmental exposures is associated with accidental releases and/or spills. If accidental releases occur, *e.g.* from containment system ruptures or malfunctions, there could be releases of large quantities of refinery gases. Other dangerous conditions associated with catastrophic release include the physical hazards of explosion and fire. Chronic exposure to refinery gases at hazardous levels is unlikely to occur since rigorous monitoring for hydrocarbon and toxic gas release as an integral component of refinery facility risk management programs (see Section 8. Human Exposure Summary, for more details).

Inorganic compounds (with the exception of asphyxiant gases such as hydrogen and nitrogen) are typically more toxic than the majority of hydrocarbons in the C1 – C4 range. For example, LC_{50} values in rats were >800,000 ppm for n-propane exposure for 15 minutes, > 570,000 ppm for isobutane exposure for 15 minutes, 276,000 ppm for n-butane exposure for 4 hours, and > 10,000 ppm for 2-butene exposure for 4 hours (Clark and Tinson, 1982; Aviado *et al*., 1977; Shugaev, 1969; Arts, 1992). In contrast, hydrogen sulfide, ammonia, methyl mercaptan, and carbon monoxide are acutely toxic at 444, 1590, 675, and 1784 ppm, respectively (Tansy *et al.*, 1981; Kapeghian *et al.*, 1982; Rose *et al.*, 1970). To further illustrate this point, see the Human Health Effects, Section 7 and Appendix 3 for information on refinery gas constituent toxicity.

The ecotoxicological hazards of refinery gases were assessed on the basis of the streams' principal components. Acute toxicity data for the three aquatic organism groups (i.e., fish, invertebrates, and algae) were gathered for those principal components and an assessment was made based on their relative hazards. The results provided an indication as to which components would be important for hazard characterization for the individual streams. In this way, a simple assessment could be made regarding relative hazards of the streams. Similar to that shown for mammalian systems, the inorganic components are often more hazardous to aquatic organisms than hydrocarbon gases. Aquatic organisms are particularly sensitive to hydrogen sulfide and ammonia, with LC/EC50 values in the low to mid parts per billion range (USEPA, 1986a; Fung and Bewick, 1980; ECB, 2000). In contrast, LC/EC50 values reported for C1 – C4 and C5 – C6 hydrocarbons generally are above one part per million (API, 2001; API, 2008a).

Table 1 presents both the hydrocarbon classes and inorganic components found in the Refinery Gases. Although ammonia appears in only one Refinery Gas TSCA definition and the mercaptans are not specifically listed in any of the Refinery Gases TSCA definitions, they are present in many streams that also contain hydrogen sulfide. Consequently, these compounds will also be designated as one of the constituents to characterize Refinery Gas hazards.

Table 1. Refinery Gas Components

Category	Refinery Gases		
Component Class	Hydrocarbons	Inorganics	Mercaptans
Component CAS Number.	Alkanes (*e.g.* propane 74-98-6)	Hydrogen sulfide 7783-06-4	Methanethiol 74-93-1
	Olefins (*e.g.* ethylene 74-85-1)	Ammonia 7664-41-7	Ethanethiol 75-08-1
	Alkadienes (*e.g.* 1,3-butadiene 106-99-0)	Hydrogen 1333-74-0	
	Alkynes (*e.g.* ethyne 74-86-2)	Nitrogen 7727-37-9	
	Aromatics (*e.g.* benzene 71-43-2)	Carbon dioxide 124-38-9	
		Carbon monoxide 630-08-0	

The carbon number range of the Refinery Gases hydrocarbons is predominantly C1 – C4. There are a few CASRN descriptions with carbon number ranges up to C5, C6, C7 and one C8 but these C4+ constituents are typically found at low concentrations in gases. Since hydrocarbon compounds containing C5, C6, C7, and C8 are found predominantly in petroleum naphthas, the hazards of these hydrocarbons have been characterized in the Gasoline Blending Streams Category. To account for any possible toxicity associated with the higher carbon number hydrocarbons, two categories of refinery gas constituents are being used for the hydrocarbon components of the refinery gases, C1 – C4 and C5 – C6. The C1 – C4 or C5 – C6 hydrocarbons typically become predominant constituents for hazard characterization in gases that contain hydrocarbons and asphyxiant gases only, with no other inorganic constitutents, such as carbon monoxide or hydrogen sulfide, present in the refinery gas stream.

Although the various gases contain toxic constituents, human health hazards would be overestimated if the overall hazards of the stream are assumed to be equal to those of the the individual constituents. The Refinery Gases often contain multiple potentially toxic inorganic and organic constutituents. Therefore, to more accurately characterize the human health hazards associated with these refinery gas streams, it is necessary to correct toxicity values (e.g. LC_{50}, repeated-dose LOAEL, etc.) associated with the gas constituents (hydrogen sulfide, ammonia, etc.) in order to reflect the dilution of that component in each specific Refinery Gas.

It should be noted that many of the components of refinery gases have extensive epidemiological and toxicological data available. It is beyond the scope of this document, and the HPV program, to thoroughly characterize the hazards associated with these compounds; that has been done elsewhere by the USEPA, NAS, ATSDR, IARC, ACGIH and other sources. The hazard information provided in this document will be limited to the HPV required SIDS endpoints, as these are the endpoints that will be used to provide the screening level hazard data requested by USEPA for these High Production Volume refinery gases.

2. REFINERY GASES CATEGORY RATIONALE

All Refinery Gases Category members contain one or more inorganic compounds in addition to gaseous hydrocarbons as listed in the stream TSCA definitions. The inorganic components of the Refinery Gases (with the exception of asphyxiant gases such as hydrogen and nitrogen) are typically more toxic than the C1 – C4 and C5 – C6 hydrocarbon components to both mammalian and aquatic organisms. Unlike other petroleum product categories (*e.g.* gasoline, diesel fuel, lubricating oils, etc.), the inorganic and hydrocarbon constituents of refinery gases can be evaluated for hazard individually to then predict the screening level hazard of the Refinery Gases Category members. The 12 refinery gas constituents identified to evaluate refinery gas category member hazards are:

- Inorganic Gases
    - Ammonia
    - Carbon Monoxide
    - Ethyl mercaptan
    - Hydrogen sulfide
    - Methyl mercaptan
- Hydrocarbon Gases
    - Benzene
    - 1,3-Butadiene
    - C1 – C4 Hydrocarbons
    - C5 – C6 Hydrocarbons
- Asphyxiant Gases
    - Carbon dioxide
    - Hydrogen gas
    - Nitrogen gas

Grouping the refinery gases into a single category is reasonable from an ecotoxicological perspective. The majority of the components in refinery gases exist in the gaseous state at typical ambient temperatures. Hence, exposure scenarios would be similar among the different category members. Based on their physical-chemical characteristics, exposure of refinery gases to aquatic organisms would require transport from the atmosphere to the water compartment. While some individual compounds in refinery gases, both organic and inorganic, are toxic to aquatic organisms in laboratory tests, the Level 1 fugacity modeling of individual constituents (see Section 5.3.1) make it clear that atmospheric releases would not result in levels of the gases in the aqueous compartment at levels sufficient to adversely effect aquatic biota. Aquatic SIDS hazard data are presented for the neat substance for selected refinery gas constituents. To assess and evaluate the potential hazards and risks of aquatic organisms to a catastrophic release of refinery gases, a conceptual exposure model was used that included inter-media transport of refinery gas constituents between the atmospheric and aquatic compartments. The constituents identified as most important for characterizing aquatic hazard were included in the conceptual exposure model.

The mammalian health hazards associated with Refinery Gases were characterized by the 12 refinery gas constituents listed above. The SIDS endpoint toxicity values are provided in Section 7, Human Health Effects. These data were used to characterize SIDS endpoints for each of the 62 Refinery Gases in the category. To accomplish this, the endpoint value (acute LC_{50}, reproductive toxicity NOAEL/LOAEL, etc.) for a specific constituent has been adjusted for concentration, using its minimum and maximum levels in each refinery gas. This adjustment for the dilution of each component in a refinery gas represents the calculated concentration of the refinery gas required to reach the toxicity value (LC_{50}, NOAEL, etc.) corresponding to the constituent in its pure state. For example, if the LC_{50} for neat (100%) hydrogen sulfide is 444 ppm, the LC_{50} for a refinery gas containing only 20% (wt./v) hydrogen sulfide would be five times more than 100% hydrogen sulfide or 2,220 ppm; *i.e.* at a gas concentration of 2200 ppm, the hydrogen sulfide concentration would be 444 ppm, equal to its LC_{50} value. In many cases, there is more than one toxic constituent in a refinery gas. In those cases, the most toxic constituent for the particular endpoint is used to characterize the hazard for each refinery stream. A more detailed explanation with examples of these calculations, along with the calculations for each of the 62 refinery gases used to determine the endpoint specific hazard values for each gas is presented in Section 7.6 and Appendix 5, which is appended as a separate Excel™ spreadsheet file to this category analysis document.

3. REFINERY GASES CATEGORY MEMBER SELECTION CRITERIA

Appendix 1 provides a complete listing of substances included in the Refinery Gases category.

The primary criteria for placing a gas into this category was the presence of inorganic compounds in the refinery stream, as had been done previously by CONCAWE in their "Other Petroleum Gases" Category. The 161 petroleum gases in the original Petroleum Gases Category were compared to the CONCAWE *"Other Petroleum Gases Category"* and overlapping CASRNs were put into the API Refinery Gases Category. The remaining, non-overlapping CASRNs were reviewed and expert judgment was used to select the remaining category member candidate list. The presence of inorganic and/or benzene/butadiene was then confirmed in historically available stream compositional data (see Appendix 2). Table 2 provides examples of Refinery Gas TSCA definitions and the corresponding compositional constituents. A complete list of the constituents associated with each category member can be found in Appendix 2.

Table 2. – Examples of Category Member Definitions and Constituents

CAS Number	Petroleum Refinery Gas Name	TSCA Definition	Refinery Gas Constituents
8006-20-0	Fuel gases, producer gas	A complex combination obtained by burning coal or coke with a restricted air supply or by blowing air and steam through incandescent coke. It consists primarily of nitrogen, carbon dioxide, carbon monoxide and hydrogen.	Hydrogen = 20 to 30%; Nitrogen = 20 to 30%; Carbon monoxide = 20 to 30%; Carbon dioxide = 20 to 30%; C1-C4 HCs = 1 to 10%.
68476-26-6	Fuel gas	A combination of light gases. It consists predominantly of hydrogen and/or low molecular weight hydrocarbons.	Hydrogen = 40 to 88%; Nitrogen = 1 to 5%; Ammonia = 0.01 to 0.2%; Hydrogen sulfide = 0.01 to 0.5%; Carbon monoxide = 0.5 to 5%; Carbon dioxide = 0.1 to 3%; C1-C4 HCs = 10 to 58%.

Table 2. – Examples of Category Member Definitions and Constituents

CAS Number	Petroleum Refinery Gas Name	TSCA Definition	Refinery Gas Constituents
68477-92-9	Gases (petroleum), dry sour, gas-concn.-unit-off	The complex combination of dry gases from a gas concentration unit. It consists of hydrogen, hydrogen sulfide and hydrocarbons having carbon numbers predominantly in the range of C1 through C3.	Hydrogen = 20 to 50%; Nitrogen = 0.5 to 10%; Ammonia = 0.1 to 5%; Hydrogen sulfide = 0.5 to 15%; Methyl mercaptan = 0.1 to 1%; Ethyl mercaptan = 0.01 to 0.5%; C1-C4 HCs = 48 to 79%.

It should be noted that Section 8(b) of the Toxic Substances Control Act required identification and registration with the Environmental Protection Agency of each "chemical substance" being manufactured, processed, imported or distributed in commerce. The substance definitions were not intended to list all constituents that would be important for hazard characterization. As can be seen in Table 2, the descriptions accompanying the CASRN of each petroleum gas are written in broad, general terms. The descriptions may contain concentration ranges, however, most CASRN descriptions provide qualitative rather quantitative analytical information. Since CASRN descriptions for refinery streams, including the refinery gases, were intentionally written to be qualitative in nature, they may or may not specifically list all of the consituents that could be present in a specific gas stream. The approximate composition (*i.e.* inorganic and hydrocarbon components) for each of the 62 refinery gases in TSCA CASRN order can be found in Appendix 2.

4. PHYSICAL-CHEMICAL PROPERTIES

Members of the Refinery Gases Category are mixtures of inorganic substances and organic compounds (hydrocarbons and non-hydrocarbons) having one to six carbon atoms. Proportions of these constituents in the refinery gas streams vary and may be a large or small fraction of the streams.

The non-hydrocarbon components (organic and inorganic) of Refinery Gases include:

- Hydrogen
- Ammonia
- Hydrogen sulfide
- Methanethiol (methyl mercaptan)
- Ethanethiol (ethyl mercaptan)
- Carbon monoxide
- Carbon dioxide
- Nitrogen

Also included in this group are two hydrocarbon substances that are considered minor components in Refinery Gases. These are not common constituents, but may be found in selected streams. Their physical-chemical characteristics were included as they may present human or ecological hazards. These are:

- 1,3-butadiene, and
- benzene.

Other C1-C4 hydrocarbon may exist in Refinery Gas Category streams, and their ranges of physical-chemical characteristics are provided below. These gases are described in more detail in the Petroleum Gases test plan (API, 2001). While the C5 – C6 hydrocarbon components in the refinery gases exist as minor constituents in these streams, they are the majority of the hydrocarbon constituents of petroleum naphthas. The physical-chemical attributes of these hydrocarbons have been thoroughly described in the gasoline blending stream category documents (API, 2008a). Ranges of physical/chemical properties from those and other sources are provided here for reference.

4.1 Physical-Chemical Endpoints

The physical-chemical endpoints in the HPV chemicals program include the following:

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

4.1.1 Melting Point

Measured melting point values for the inorganic constituents in refinery gases are given below.

Non-Hydrocarbon Constituents:	**Melting Point °C**	**Reference**
Hydrogen	-259	Budavari (1996)
Ammonia	-77.7	Budavari (1996)
Hydrogen sulfide	-85.5	Budavari (1996)
Methanethiol	-123	O'Neil (2001)
Ethanethiol	-148	Lide and Milne (1994)
Carbon monoxide	-205	Budavari (1996)
Carbon dioxide	-56.5	Lide (1994)
Nitrogen	-210	Budavari (1996)
Organic Constituents:		
Benzene	5.5	Budavari (1996)
1,3-butadiene	-109	Budavari (1996)

Other hydrocarbon gases:
C1 to C4 and C5 to C6 hydrocarbons of various classes (alkanes, alkenes, naphthenes) and isomeric structures have melting points that range from -189.7 °C to -138.4 °C (API, 2001) and from -130 °C to -95 °C (USEPA, 2000a), respectively.

4.1.2 Boiling Point

Estimated or measured boiling point values for the inorganic constituents in refinery gases are given below.

Non-Hydrocarbon Constituents:	**Boiling Point °C**	**Reference**
Hydrogen	-252.8	Budavari (1996)
Ammonia	-33	Budavari (1996)
Hydrogen sulfide	-60.3	Budavari (1996)
Methanethiol	5.95	O'Neil (2001)
Ethanethiol	35.1	Lide and Milne (1994)
Carbon monoxide	-191.5	Budavari (1996)
Carbon dioxide	-78.5	Lide (1994)
Nitrogen	-196	Budavari (1996)

Organic Constituents:

Benzene	80.1	Budavari (1996)
1,3-butadiene	-4.5	Budavari (1996)

Other hydrocarbon gases:
C1 to C4 and C5 to C6 hydrocarbons of various classes (alkanes, alkenes, naphthenes) and isomeric structures have boiling points that range from -164 °C to – 0.5 °C (API, 2001) and from 36 °C to 69 °C (USEPA, 2000a), respectively.

4.1.3 Vapor Pressure

Estimated or measured vapor pressures for the inorganic constituents in refinery gases are given below.

Non-Hydrocarbon Constituents:	**Vapor Pressure (hPa @ temp)**	**Reference**
Hydrogen	1,653,198 @ 25°C	Ohe (1976)
Ammonia	10,013 @ 25°C	Daubert and Danner (1989)
Hydrogen sulfide	20,798 @ 25°C	Daubert and Danner (1989)
Methanethiol	20,665 @ 25°C	Daubert and Danner (1989)
Ethanethiol	529 @ 25°C	Daubert and Danner (1989)
Carbon monoxide	20,664,972 @ 25°C	USEPA, 2000a
Carbon dioxide	64,395 @ 25°C	Daubert and Danner (1989)
Nitrogen	1,013 @ -196 °C	Weast (1984)
Organic Constituents:		
Benzene	126 @ 25°C	Daubert and Danner (1989)
1,3-butadiene	2,813 @ 25°C	Daubert and Danner (1989)

Other hydrocarbon gases:
C1 to C4 and C5 to C6 hydrocarbons of various classes (alkanes, alkenes, naphthenes) and isomeric structures have vapor pressures that range from 3796 hPa to 350,000 hPa (API, 2001) and from 201 hPa to 685 hPa (USEPA, 2000a), respectively.

4.1.4 Octanol:Water Partition Coefficient (Log Kow)

Estimated or measured log Kow values for the inorganic constituents in refinery gases are given below.

Non-Hydrocarbon Constituents:	**Log Kow**	**Reference**
Hydrogen	N/A	
Ammonia	-1.14	BASF AG (1992)
Hydrogen sulfide	0.45	BASF AG (1992)
Methanethiol	0.65	Abraham et al. (1994)
Ethanethiol	1.27	USEPA, 2000a
Carbon monoxide	1.78	USEPA, 2000a
Carbon dioxide	0.83	USEPA, 2000a
Nitrogen	0.67	Hansch et al. (1995)
Organic Constituents:		
Benzene	2.13	Hansch et al. (1995)
1,3-butadiene	1.99	Hansch et al. (1995)

Other hydrocarbon gases:
C1 to C4 and C5 to C6 hydrocarbons of various classes (alkanes, alkenes, naphthenes) and isomeric structures have partition coefficients (Log Kow) that range from 1.09 to 2.8 (API, 2001) and from 3.4 to 3.9 (USEPA, 2000a), respectively.

4.1.5 Water Solubility

Estimated or measured water solubility values for the inorganic constituents in refinery gases are given below.

Non-Hydrocarbon Constituents:	Water Solubility mg/L	Reference
Hydrogen	1.62	Venable and Fuwa (1922)
Ammonia	340,000	Budavari (1996)
Hydrogen sulfide	3,980	Kirk-Othmer (1991)
Methanethiol	15,400	Hine and Mookerjee (1975)
Ethanethiol	15,600	Wakita et al. (1986)
Carbon monoxide	24,582	USEPA, 2000a
Carbon dioxide	1,480	USEPA, 2000a
Nitrogen	18,100	USEPA, 2000a
Organic Constituents:		
Benzene	1,790	May et al. (1983)
1,3-butadiene	735	McAuliffe (1966)

Other hydrocarbon gases:
C1 to C4 and C5 to C6 hydrocarbons of various classes (alkanes, alkenes, naphthenes) and isomeric structures have water solubility values that range from 24 mg/L to 61 mg/L (API, 2001) and from 9.5 to 38 mg/L (USEPA, 2000a), respectively.

4.2 Assessment Summary for Physical-Chemical Endpoints

The different chemicals constituting refinery gases are shown to have extremely low melting and boiling points. They also have high vapor pressures and low octanol/water partition coefficients. The aqueous solubility of these components varies, and can widely range from low part per million (hydrogen gas) to several hundred thousand parts per million (ammonia).

5. ENVIRONMENTAL FATE

As noted in previous sections, members of the Refinery Gases Category are characterized as mixtures of inorganic substances and hydrocarbon compounds having one to six carbon atoms. Proportions of these constituents in the refinery gas streams vary and may make up a significant or minor portion in these streams.

When a substance such as one of the Refinery Gases streams is released into the environment, the individual constituents separate and partition to the different environmental compartments in accordance with their own physical-chemical properties. The ultimate fate of the individual components in Refinery Gases are influenced by both abiotic and biotic processes, and the relative importance of these processes will depend upon the environmental compartment to which the individual components partition.

The individual streams within the Refinery Gases Category are not uniquely different among themselves. The key difference is the proportions of several common constituents in their makeup. By understanding the environmental fate characteristics of these individual components, an overall assessment of the entire stream is possible. Therefore, the environmental fate attributes of the key individual organic and inorganic constituents in Refinery Gases are described in the following sections.

5.1 Environmental Fate Endpoints

The USEPA has selected the following environmental fate endpoints by which these substances may be characterized.

photodegradation,

stability in water (hydrolysis),
environmental distribution (fugacity), and
biodegradation.

In determining these fate characteristics for constituents in Refinery Gases, the USEPA's collection of physical-chemical and environmental fate models in EPI Suite™ (USEPA, 2000a) were used estimate the properties of photodegradation, stability in water, and environmental distribution. Measured data, when available, were also included in the assessment. Biodegradation was examined for these substances in light of their physical-chemical properties, their capacities to undergo microbial oxidation/reduction reactions, or their existence in different oxidation states brought about by microbial populations.

5.1.1 Photodegradation

5.1.1.1 Direct Photodegradation

A prerequisite for direct photodegradation is the ability of one or more bonds within a chemical to absorb ultraviolet (UV)/visible light in the 290 nm to 750 nm wavelength range. Light wavelengths longer than 750 nm do not contain sufficient energy to break chemical bonds, while wavelengths below 290 nm are shielded from the earth by the stratospheric ozone layer (Harris, 1982a).

Direct photodegradation of the hydrocarbon components in Refinery Gases is not expected to be an important fate process for these constituents. Saturated hydrocarbons (paraffins and naphthenes), olefins with one double bond, and single ring aromatics do not absorb appreciable light energy above 290 nm. Therefore direct photodegradation would not be expected to occur for these compounds. Additionally, butadiene does not absorb appreciable light energy above 290 nm to effect transformation (ACC, 2004).

The predisposition for direct photolysis of other constituents (non-hydrocarbons) in Refinery Gases depends on the specific substance. Therefore, each component is discussed separately.

Hydrogen. Hydrogen gas (H_2) has such low density that it easily escapes from the earth's gravitational pull. Therefore it is only a minor constituent of the atmosphere (Boikess and Edelson, 1978). The H─H bond has a large bond energy so dissociation only occurs at extreme temperatures (e.g., >2000°K). This property makes hydrogen gas un-reactive in the troposphere.

Ammonia. Ammonia is transparent in the visible and near-ultraviolet regions of the electromagnetic spectrum, and will not undergo any primary photochemical reactions under normal tropospheric conditions (NRC, 1979).

Hydrogen Sulfide. Hydrogen sulfide does not absorb solar radiation reaching the troposphere. Therefore, it does not undergo photolysis or react photochemically with oxygen (NRCC, 1981).

Methanethiol. Methanethiol is not expected to undergo direct photodegradation due to the lack of absorption in the UV spectrum (>290 nm) (Sheraton and Murray, 1981).

Ethanethiol. Ethanethiol does not absorb light at wavelengths >290 nm and therefore is not expected to be susceptible to direct photolysis by sunlight (NLM, 2006).

Carbon monoxide. Carbon monoxide is a stable compound, with a very high bond energy between the carbon and oxygen atoms (Boikess and Edelson, 1978). It is not known to show spectral absorbance in the 290 – 750 nm range. Therefore, direct photodegradation is not likely to occur.

Carbon Dioxide. Carbon dioxide is a stable compound (Boikess and Edelson, 1978). It is a relative minor constituent in the atmosphere. It shows no spectral absorbance in the 290 – 750 nm range, thus direct photodegradation is not likely to occur.

Nitrogen. Nitrogen gas (N_2) in the atmosphere is relatively non-reactive due to its strong bond. Therefore, direct photodegradation is not likely to occur. The atmosphere serves as a reservoir from which nitrogen is constantly removed by the action of electrical discharge and nitrogen-fixing bacteria and algae. Atmospheric inputs of nitrogen gas come from reduction of nitrates and nitrites, and the anaerobic decomposition of organic matter (Sawyer and McCarty, 1978).

5.1.1.2 Indirect Photodegradation

Substances in Refinery Gases that volatilize to air may undergo a gas-phase oxidation reaction with photochemically produced hydroxyl radicals (OH^-). Atmospheric oxidation as a result of hydroxyl radical attack is not direct photochemical degradation, but rather indirect degradation (Schwarzenbach et al, 2003). The atmospheric oxidation potential (AOP) of the major constituents in Refinery Gases was estimated using AopWin (atmospheric oxidation program for Microsoft Windows), a subroutine in the EPI Suite™ (USEPA, 2000a) models and used by the US EPA OPPTS (Office of Pollution Prevention and Toxic Substances). This program calculates a reaction rate constant (cm^3/molec-sec) and a chemical half-life (hour or days) of a compound based upon average atmospheric concentrations of hydroxyl radicals (1.5×10^6 OH^-/cm^3) and a 12-h day at 25°C.

Indirect photodegradation of the hydrocarbon components in Refinery Gases can be an important fate process for these constituents. In general, half lives decrease with increasing carbon chain length. Half lives for this fraction of Refinery Gases ranged from 960 days (methane) to 0.16 days (butadiene). The constituents of the C5 – C6 hydrocarbon fraction have photodegradation half-lives of approximately two days.

The tendency for indirect photodegradation of constituents of the inorganic fraction in Refinery Gases depends on the specific substance. Therefore, each inorganic component is discussed separately. The AopWin program is not appropriate for all the inorganic substances in this list. For these substances an overview of their potential to undergo reactions with hydroxyl radicals was taken from general references.

Hydrogen. As noted for direct photodegradation potential, hydrogen gas (H_2) has such low density that it easily escapes from the earth's gravitational pull and is only a minor constituent of the atmosphere (Boikess and Edelson, 1978). The H─H bond has a large bond energy so dissociation only occurs at extreme temperatures (e.g., >2000°K). This property makes hydrogen gas un-reactive in the troposphere.

Ammonia. Although the AopWin program could not provide rate constants or half lives for the interaction of ammonia and hydroxyl radicals, McConnell (1973) concluded that this reaction is the most important destruction mechanism for ammonia in the troposphere. Hydroxyl-ammonia reaction rate constants have been measured by several investigators and presented by NRC (1979). Perry et al. (1976) calculated that for a hydroxyl radical concentration of 3×10^6 molecules/cm^3 and a measured rate constant of 1.64×10^{-13}, the half life for ammonia in the troposphere was approximately 16 days.

Hydrogen sulfide. The AopWin program could not provide rate constants or half lives for the interaction of hydrogen sulfide and hydroxyl radicals. NRCC (1981) described the primary transformation of hydrogen sulfide in the atmosphere as oxidation by oxygen containing radicals to sulfur dioxide and sulfates. For hydrogen sulfide, ECB (2000) cited a OH radical rate constant of 4.8×10^{-12} cm^3/molecule-sec and a half life of approximately 80.2 hours.

Methanethiol. The rate constant for the vapor-phase reaction of methanethiol with photochemically-produced hydroxyl radicals is $3.29X10^{-11}$ cu cm/molecule-sec at 25 °C (Atkinson, 1989). This corresponds to an atmospheric half-life of about 11.7 hours at an atmospheric concentration of 5×10^5 hydroxyl radicals/cm^3. Sulfur dioxide (SO_2) is a major product of this reaction.

Ethanethiol. The rate constant for the vapor-phase reaction of ethanethiol with photochemically-produced hydroxyl radicals is $4.68X10^{-11}$ cu cm/molecule-sec at 25 °C (Atkinson, 1989). This corresponds to an atmospheric half-life of about 10 hours at an atmospheric concentration of 5×10^5 hydroxyl radicals/cm^3.

Carbon monoxide. The AopWin model calculated an overall OH^- rate constant of 6.9 x 10^{-9} cm^3/molecule-sec, thus giving a half life of 1559 days.

Carbon dioxide. As noted for direct photodegradation, carbon dioxide is chemically stable and is a relatively minor constituent in the atmosphere (Boikess and Edelson, 1978).

Nitrogen. Nitrogen gas (N_2) in the atmosphere is relatively non-reactive due to its strong bond. Therefore, indirect photodegradation is not likely to occur. Atmospheric nitrogen is removed by nitrification processes (Sawyer and McCarty, 1978).

5.1.2 Stability in Water (Hydrolysis)

Compound types that are known to hydrolyze include alkylhalides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Harris, 1982b). The hydrocarbon and non-hydrocarbon constituents in Refinery Gases do not contain the functional groups or chemical linkages known to undergo hydrolysis reactions. Therefore hydrolysis will not play an important role in the environmental fate for the components in Refinery Gas streams.

5.1.3 Environmental Distribution (Fugacity)

Equilibrium models can provide information on where a chemical is likely to partition in the environment. These data are useful in identifying environmental compartments that could potentially receive a released chemical. A widely used fugacity model is the EQC (Equilibrium Criterion) model (Mackay et al., 1996, 1997). In its guidance document for HPV data development, the USEPA states that it accepts Level I fugacity data as an estimate of chemical distribution values. The EQC model is a Level I model that describes the equilibrium distribution of a fixed quantity of conserved (i.e., non-reacting) chemical at steady state within a closed environment with assumed volumes of air, water, soil and sediment. The model assumes the chemical becomes instantaneously distributed to an equilibrium condition using physical-chemical properties to quantify the chemical's behavior. The model does not include degrading reactions, advective processes or inter-media transport between compartments.

Results of Level I models are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical is likely to partition in the environment. The gases in greatest proportion in the Refinery Gases streams (H_2, N_2, CO_2) typically have very low boiling points. These substances exist as gases at most ambient environmental temperatures. While all of the non-hydrocarbon constituents would be expected to partition to the atmosphere, some have high levels of water solubility and may cause adverse effects on aquatic organisms. Therefore, these substances (hydrogen sulfide, methanethiol, ethanethiol, and ammonia) were assessed for their environmental distribution using the Mackay et al. (1996, 1997) EQC model. Hydrocarbon gases (C1 to C4) along with benzene and 1,3-butadiene also were assessed for their potential environmental distribution.

Table 3. Results of EQC Level 1 Environmental Distribution Modeling of Important Components in Refinery Gases.

	Environmental Compartment, Percent Distribution					
Refinery Gas Constituent	**Air**	**Water**	**Soil**	**Sediment**	**Suspended Partilcles**	**Biota**
Non-hydrocarbon Fraction						
hydrogen sulfide	100%	<0. 1%	<0.1%	<0.1%	<0.1%	<0.1%
methanethiol	99.2%	0.77%	<0.1%	<0.1%	<0.1%	<0.1%
ethanethiol	98.2%	1.7%	<0.1%	<0.1%	<0.1%	<0.1%
ammonia	88.0%	11.9%	<0.1%	<0.1%	<0.1%	<0.1%
Hydrocarbon Fraction						
1,3-butadiene	100%	<0.1%	<0.1%	<0.1%	<0.1%	<0.1%
benzene	99.0%	0.88%	<0.1%	<0.1%	<0.1%	<0.1%
C1 to C4 alkanes	100%	<0.1%	<0.1%	<0.1%	<0.1%	<0.1%
C5 to C6 alkanes	99.8 – 100%	<0.1%	<0.1 – 0.2	<0.1%	<0.1%	<0.1%

The Level 1 modeling show that these constituents would overwhelmingly partition to the air. For ammonia approximately 12% may partition to water.

5.1. Biodegradation

Some of the non-hydrocarbon fraction of the Refinery Gases would not be expected to biologically degrade as these substances do not contain the chemical linkages necessary for microbial metabolism. For this reason, hydrogen, nitrogen, and carbon dioxide would not be susceptible to biodegradation. Furthermore, carbon dioxide is the final product in the biological mineralization of organic compounds. In contrast, ammonia can be readily oxidized to nitrite under aerobic conditions by autotrophic nitrifying bacteria (Sawyer and McCarty, 1978). Carbon monoxide has been reported to be microbially oxidized to CO_2 in pure cultures by a number of microbial species. It was also shown to be rapidly converted to CO_2 by indigenous soil microbial communities (Bartholomew and Alexander, 1979). Methanethiol can be both evolved and consumed in nature. It is produced by a variety of organisms through the decay of sulfur-containing organic matter under anoxic conditions (Kiene and Capone, 1988). Methanethiol is known to undergo both aerobic and anaerobic biodegradation, but Lomans et al. (1999) reported methanogenesis was the major mechanism of methanethiol consumption under an anoxic environment. Visscher and Taylor (1993) showed that a pure culture of *Thiobacillus* sp. grown in the presence of dimethyl sulfide oxidized a range of alkylthiols including methanethiol and ethanethiol. Hydrogen sulfide does not biodegrade *per se*, but bacteria play an important role in the cycling of sulfur in the environment. The reduction of sulfate to hydrogen sulfide occurs in anoxic environments by anaerobic bacteria (Sawyer and McCarty, 1978). Conversely, hydrogen sulfide can be

oxidized to elemental sulfur and sulfate by a number of bacteria (USEPA, 1986a). Much of this cycling of sulfur occurs in sediments at the boundary layer between oxic and anoxic conditions (USEPA, 1986a).

Biodegradation of the hydrocarbon components in refinery gases may occur in soil and water. Gaseous hydrocarbons are widespread in nature and numerous types of microbes have evolved which are capable of oxidizing these substances as their sole energy source (Fuerst and Stephens, 1970; Stephens et al, 1971; O'Brien and Brown, 1967). Although volatilization is the predominant behavior for these gases, sufficient aqueous solubility and bioavailability is exhibited by these compounds. The use of gaseous carbon sources for cell growth is common among autotrophic organisms (Vestal, 1984). Higher chain length hydrocarbons typical of naphtha streams also are known to inherently biodegrade in the environment (API, 2008a).

5.2 Assessment Summary for Environmental Fate

Refinery gases are made up of a diverse group of individual inorganic and organic compounds, and their environmental fate characteristics are governed to a great extent by their physical-chemical attributes. All components were shown to partition to the air, where interaction with hydroxyl radicals may be important or have no influence on their fate. Many of the gases are chemically stable and may be lost to the atmosphere or simply become involved in the recycling of their atoms. Some show substantial water solubility, but their volatility will eventually cause these gases to enter the atmosphere.

6. ENVIRONMENTAL EFFECTS

6.1 Aquatic Toxicity

In context of the factors affecting potential exposure of aquatic organisms to Refinery Gases acute toxicity from a catastrophic release is considered the primary concern. While chronic effects may be observed in laboratory tests where long-term exposures can be maintained, such exposures from fugitive environmental releases is not likely to impact aquatic systems. As described in previous sections, these substances exist in the gaseous phase at the refinery and are contained in closed systems. If released inadvertently, these substances would partition to the air and are not likely to enter aquatic environments. Furthermore, they are used primarily as intermediates in other refinery processes or are consumed on-site as fuel gas for energy.

N_2, H_2, CO_2, and CO are not known to be directly toxic to aquatic organisms. While direct release of these substances to water (e.g., bubbled through the water column) may result in oxygen displacement potentially resulting in death due to asphyxiation, no information on their being directly toxic to aquatic life was found. Therefore they were not considered further in this evaluation. However, other constituent substances in refinery gases have well documented aquatic hazards and were considered potential toxic constituents in these streams. These include ammonia, hydrogen sulfide, methanethiol, ethanethiol, benzene, and C1-C4 hydrocarbons. Available aquatic toxicity data for these substances were tabulated and presented below.

6.2 Aquatic Endpoints – Acute Toxicity

The HPV Chemical Test Program includes acute toxicity to a freshwater fish, an invertebrate (*Daphnia magna*), and an alga. To determine the aquatic hazard of the most toxic components in Refinery Gases to these organisms, data cited in USEPA's ECOTOX database (USEPA, 2007a), USEPA's National Water Quality Criteria documents (USEPA, 1986b), and the European Chemicals Bureau ESIS Database (ECB, http://ecb.jrc.ec.europa.eu/esis/) were reviewed. Ranges of toxicity endpoints (i.e., LC50, EC50 values) were noted for the various constituents in Refinery Gases. When toxicity data was lacking, the ECOSAR model in EpiSuite™ (USEPA, 2000a) was used to derive estimated LC/EC50 values.

A comparison of the aquatic hazard data revealed seven principle constituents in Refinery Gases that exhibited the greatest potential to cause adverse effects in aquatic organisms. These are,

- ammonia,

- hydrogen sulfide,
- methanethiol,
- ethanethiol
- benzene
- C1 – C4
- C5 – C6 hydrocarbons.

1,3-Butadiene has not been separated from the C1-C4 fraction because it shows aquatic hazards similar to other C4 hydrocarbons (see Table 10 and Appendix 3). The Refinery Gas constituents of interest show the following ranges of toxicity values for fish, invertebrates, and algae.

Table 4. Acute Toxicity Data for Refinery Gas Constituents to Aquatic Organisms.

	Range of Toxicity Endpoint Values		
	Fish LC50, mg/L	**Invertebrate EC50, mg/L**	**Algae EC50, mg/L**
ammonia[1]	0.083 – 4.6	0.53 – 22.8	no data
hydrogen sulfide[2]	0.007 – 0.2	0.022 – 1.07	no data
methanethiol[3]	0.5≤LC50≤1.75	1.32 ≤EC50≤ 2.46	no data
ethanethiol[4]	no data	90 – 280	No data
Benzene[5]	5.3 – 35.7	59.6 – 682	29
C1 – C4 hydrocarbons[6]	11.3 – 167	12.7 – 164	1.3 – 95.7
C5 – C6 hydrocarbons (naphthas)[7]	3.9 – 9.5	4.6 – 10.7	3.1 – 7.0

Data Sources:
[1] USEPA (1986b)
[2] Fung and Bewick (1980); Smith et al. (1976); ECB (2000)
[3] Haydu et al. (1952); Elf Atochem S.A. (2000)
[4] USEPA (2000a); Maas (1990)
[5] DeGraeve, et al. (1982); Brooke (1987); MacLean and Doe (1989); Eastmond et al. (1984); Galassi et al., (1988)
[6] API (2001)
[7] USEPA (2000a)

The data in Table 4 shows ammonia and hydrogen sulfide to be the most hazardous of the major constituents in refinery gases. However, differential solubility levels of the various components may influence their partitioning to water following an atmospheric release.

To evaluate whether water concentrations of these substances would reach acutely toxic levels following an atmospheric release of refinery gases, a Level 3 fugacity model was run on each individual component. Input data

included specific physical-chemical values for boiling point, melting point, vapor pressure, octanol-water partition coefficient, and water solubility for each substance. The model was run using an emission rate of 1000 kg/hr to the atmosphere for one hour. The concentration of each substance then was calculated assuming an aquatic compartment of 2×10^{11} m^3 (equivalent to 2×10^{14} L). While these substances typically do not constitute 100% of any refinery gas, the model cannot assess mixtures of chemicals. Thus, the resulting calculations reflect the concentrations following release of these substances in their pure state. Table 5 illustrates the results of the Level 3 model and the estimated water concentration.

Table 5. Results of Level 3 Fugacity modeling and Calculation of Water Concentrations

	Ammonia	Hydrogen sulfide	Methane-thiol	Ethane-thiol	Benzene	Methane	Pentane
Water Solubility, mg/L	340,000	3,980	15,400	15,603	1,790	22	38
Henry's LC, atm-m^3/mole	5.0×10^{-5}	8.6×10^{-3}	3.1×10^{-3}	4.5×10^{-3}	5.6×10^{-3}	6.6×10^{-1}	1.3
Mass amount in compartment, %							
air	96	100	99	99	99	100	100
water	3.5	0.01	0.70	0.49	0.51	<0.01	<0.01
soil	0.3	<0.01	0.05	0.05	0.13	<0.01	0.01
sediment	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Half Life in Compartment, hr							
air	100000	100000	7.8	5.5	209	37400	65
water	360	360	360	360	200	360	208
soil	720	720	720	720	1800	720	416
sediment	3240	3240	3240	3240	8100	3240	1870
Calculated concentration in water, mg/L							
	1.76×10^{-7}	6.45×10^{-10}	3.48×10^{-8}	2.43×10^{-8}	2.53×10^{-8}	1.73×10^{-10}	7.25×10^{-11}
Toxicity Conclusions:	no toxicity	no toxicity	no toxicity	no toxicity	no toxicity	no toxicity	no toxicity

From the data shown by the Level 3 fugacity model, very little of the individual substances will partition to the water when emissions are to the atmosphere. Likewise, the concentrations of these substances would be expected to be extremely low and below levels found to be acutely toxic in laboratory studies.

6.4 Assessment Summary for Environmental Effects

Several of the constituents in refinery gases were shown to be highly hazardous to aquatic organisms in laboratory toxicity tests where exposure concentrations can be maintained over time. Hydrogen sulfide was shown to be the most toxic constituent to fish (LC50 ranged 0.007 to 0.2 mg/L) and invertebrates (EC50 ranged 0.022 to 1.07 mg/L), although several LC/EC50 values for ammonia also were below 1 mg/l for these organisms (0.083 to 4.6 mg/L and 0.53 to 22.8 mg/L, respectively). Given the physical-chemical characteristics of the refinery gases and the confined production and use within refineries, potential exposures to aquatic organisms would be greatest from accidental catastrophic releases. Fugitive emissions in refineries would not be expected to impact aquatic systems. Based on a simple conceptual exposure model analysis, emissions of refinery gases to the atmosphere would not likely result in acutely toxic concentrations in adjacent water bodies because such emitted gases will tend to remain in the atmosphere.

7. HUMAN HEALTH EFFECTS

For the Refinery Gases Category, category member human health hazard potential has been evaluated by characterizing refinery gas inorganic and organic constituent hazard, then comparing hazard contribution by accounting for constituent concentration. As previously mentioned, although some of the constituents in the category are quite toxic by themselves, it would be overestimating the human health hazard of any one stream to assume that the toxicity of the stream is equal to that of the pure constituent. The Refinery Gases may contain multiple inorganic compounds as well as hydrocarbon components, which serve to dilute the concentration of any one constituent. Therefore to more accurately characterize the potential human health hazards associated with these gases, it is necessary to correct the pure (100%) constituent toxic potential, such as hydrogen sulfide or ammonia, to the concentrations of those constituents in each specific Refinery Gas. Since the streams are not 100% of any one constituent, calculations to account for this dilution effect were made for all constituents present in each refinery gas category member. The most toxic constituent for each human health endpoint was then selected to characterize the hazard for that stream for that endpoint. Please see Section 7.6 for more details on the hazard characterization method. Table 12 presents the calculated values for each human health endpoint for each of the 62 refinery gas category members. Calculations to determine the appropriate component to characterize the hazard for each mammalian endpoint in each refinery gas are presented in the EXCEL™ spreadsheet (Refinery Gases Appen 5 dilution calcs – hlth endpts.xls) submitted with this category analysis document.

The following sections summarize existing USEPA HPV SIDS endpoint key studies for ammonia, carbon monoxide, hydrogen sulfide, methanethiol, ethanethiol, benzene, 1,3-butadiene, C1 – C4 hydrocarbon fraction and C5 – C6 hydrocarbon light naphtha hydrocarbon fraction. The key studies selected are tabulated by endpoint in Appendix 3. The key studies for the C1 – C4 hydrocarbon fraction were selected after review of existing toxicity data on individual C 1 – C4 hydrocarbons, *e.g.* ethane, propane, butane, etc. After review of existing data on the individual C1 – C4 HCs, the most toxic hydrocarbon was selected to represent the C1 – C4 HC fraction toxicity for each endpoint. The most toxic individual C1- C4 HC varied by endpoint. By selecting one hydrocarbon to represent the entire C1-C4 HC fraction, for toxicity assessment it is assumed that the entire C1- C4 fraction concentration in each HC-containing refinery gas is 100% of the selected individual HC for a specific mammalian SIDS endpoint. For example, the most toxic C1-C4 HC for repeated-dose toxicity is 2-butene; for predicting repeated-dose toxicity, a refinery gas containing 5 – 10% C1- C4 HCs is assumed to contain 5 – 10% 2-butene, without other HCs present. Please see Appendix 4 for a list of the C1 – C4 data evaluated for key study selection. For the C5 – C6 light naphtha hydrocarbon fraction, endpoint values were read across from SIDS endpoint values presented in detail in the Gasoline Blending Stream Category Analysis Document previously submitted to USEPA (API, 2008a). Whenever possible, naphtha light ends fraction testing conducted in compliance with the Clean Air Act 211(b) testing requirements were read across to the C5 – C6 hydrocarbons. For the three inorganic compounds that are simple asphyxiants (hydrogen, nitrogen and carbon dioxide), the human health SIDS endpoints are not provided. If hydrogen, nitrogen, or carbon dioxide are present in a specific refinery gas, it is assumed that toxicity would only occur at or above asphyxiant levels, *i.e.*, levels that reduce the pO_2 levels to below 132 torr (ACGIH, 2008; NIOSH 1980) to create an exposure atmosphere that does not meet the minimum requirement of 19.5% oxygen at sea level to adequately support human respiration (NIOSH 1987; McManus, 1999).

7.1 Acute Toxicity

Ammonia[1]

The acute toxicity of ammonia was determined in male albino ICR mice. Twelve mice per group were exposed to 0, 1190, 1340, 2130, 3440, 3950, 4220, 4490, or 4860 ppm ammonia for one hour and observed for 14 days following exposure. Immediate clinical signs of toxicity included excitation/escape behavior rapid vigorous tail revolution,

[1] Ammonia is a well studied chemical with several comprehensive reviews available, including an ATSDR Toxicological Profile which can be found at http://www.atsdr.cdc.gov/toxprofiles/tp126.html.

blinking and scratching (presumably due to eye and nasal irritation), and dyspnea. Longer term signs of toxicity included reduced activity, tremors, ataxia, clonic convulsion, frothing, final toxic extensor seizure, and death. All deaths occurred at concentrations ≥ 3950 ppm. The one hour LC_{50} was calculated to be 4230 ppm (Kapeghian *et al*., 1982). This study was used as one of two key studies to derive the Acute Exposure Guideline Level – 3 for ammonia; AEGL – 3 is the concentration of a substance that is immediately dangerous to human health (NRC, 2007). To make this one hour LC_{50} more comparable to the four hour LC_{50} of the other refinery gas constituents, the one hour value was converted to a four hour LC50 using the NIOSH Immediately Dangerous to Life and Health (IDLH) methods (NIOSH, 1994). The NIOSH method corrects to a 30 minute exposure, so using the one hour LC50 in place of the 30 minute LC_{50} concentration provides a very conservative estimate of a four hour LC50. The calculated four hour LC_{50} ~ 1590 ppm (calculated value = 1586 ppm).

One hour (male ICR mouse) LC_{50} for both sexes = 4230 ppm
Four hour (male ICR mouse) LC_{50} = 1590 ppm (calculated)

Carbon monoxide[2]
In an acute toxicity study, 4 – 12 male Sprague-Dawley rats per group (number of animals varied per group) were exposed to 1600, 1800, 2000 or 2200 ppm carbon monoxide for 4 hours under various atmospheric pressures. Carbon monoxide concentrations were continuously monitored by an IR spectrophotometer or gas chromatograph. Increasing atmospheric pressure did not significantly alter the LC_{50} (data not presented). In general, all animals lost consciousness during the first 1-2 hr of exposure to CO. Immediately after the exposures, cardiac blood samples from dead animal were collected and analyzed for carboxyhemoglobin concentration. Mortality by dose was 1/4 (#dead/#in group), 2/4, 4/8, and 11/12 for 1600, 1800, 2000 or 2200 ppm carbon monoxide, respectively. The LC50 values and their 95% confidence limits were calculated by the method of Litchfield and Wilcoxon. The male rat LC50 was 1807 ppm with 95% confidence limits of 1598 – 1956 ppm (Rose *et al*., 1970).

Four hour (male Sprague-Dawley rat) LC50 = 1807ppm

Hydrogen sulfide[3]
The inhalation acute toxicity of hydrogen sulfide was assessed in male and female Sprague-Dawley rats. Five rats/sex/group were exposed for 4 hours to 0 (air control), 400, 440, 475, 500, 525, 554, or 600 ppm hydrogen sulfide and observed for 14 days and examined for gross pathology, such as general or local hemorrhage and adhesions. Mortality and visually apparent behavior such as exploring, huddling, preening, and obvious distress were noted during the 4 hr exposure. The rats were deprived of food and water during exposure. Animals which survived the first 24 hours after exposure survived to the end of the 14 day exposure period. Some lethality was observed at all doses. The number of deaths per group were 0/10, 3/10, 3/10, 7/10, 8/10, 8/10, 9/10, and 10/10 for 0 (air control), 400, 440, 475, 500, 525, 554, or 600 ppm hydrogen sulfide, respectively. The calculated LC_{50} was 444 ppm, with a confidence interval of 416 – 473 ppm (Tansy *et al*., 1981).

Four hour (male and female Sprague-Dawley rat) LC_{50} = 444 ppm

Methanethiol
An acute study equivalent to OECD Guideline 403 was conducted on the mercaptan methanethiol. Each dose group consisted of 5 male and 5 female Sprague-Dawley rats, which were combined for a 4-h exposure or sham exposure to air in a customized 75-l glass chamber and then separated for observation over the subsequent 14-day period. Exposure concentrations were 400, 600, 650, 680, 680, 700, 800 ppm. Animals from any group that died during the 14-day period were examined for gross pathology, such as general or local hemorrhage and adhesions, and the survivors were sacrificed and examined as well. Mortality and such visually apparent behaviour as exploring, huddling, preening, and obvious distress were noted during the courses of the 4-hour exposures and sham exposures.

[2] Carbon monoxide is a well studied chemical with several comprehensive reviews available, including the USEPA Air Quality Criteria for Carbon Monoxide which can be found at http://www.epa.gov/ncea/pdfs/coaqcd.pdf.
[3] Hydrogen sulfide is a well studied chemical; for more information see ATSDR Toxicological Profile for Hydrogen Sulfide at HTTP://WWW.ATSDR.CDC.GOV/TOXPROFILES/TP114.HTML#BOOKMARK16

The rats were deprived of food and water during actual exposure or sham exposure. LC50 values and 95% confidence limits were estimated by the classical method of Litchfield and Wilcoxon. The LC_{50} from this study was 675 ppm, with a confidence interval of 643 – 709 ppm (Tansy *et al*, 1981).

Four hour (male and female Sprague-Dawley rat) LC_{50} = 675 ppm

Ethanethiol
Fairchild and Stokinger (1958) exposed groups of 10 Swiss-derived male mice (body weight 32 25-28 g) to 2600, 3150, 3573, 4438, or 4832 ppm ethyl mercaptan for 4-hours, followed by a 15- 33 day observation period. Vapor generation was achieved by either bubbling a stream of nitrogen gas through a midget fritted-glass bubbler, which contained liquid ethyl mercaptan, or by passage of nitrogen into a borosilicate glass nebulizer containing the ethyl mercaptan. Desired exposure concentrations were maintained in a 18-L glass chamber by varying the ratio of volume flow of compressed air and compressed nitrogen. Ethyl mercaptan concentrations during exposure periods were measured by absorption of vapors in either isopropyl alcohol or acetone containing an excess of silver nitrate and titrating the uncombined silver amperometrically. Chamber concentrations during tests were uniform after the first 30 minutes; mean variation for all exposures was approximately 4%. Clinical signs included increased respiration and restlessness (hyperactivity), incoordinated movement, staggering gait, muscular weakness, partial skeletal muscle paralysis beginning in the hind limbs, light to severe cyanosis, tolerance of a prone position, and mild to heavy sedation. Animals exposed to "maximal lethal concentrations" typically died from respiratory arrest during exposure or shortly after removal from the chamber. Animals exposed to "minimal lethal concentrations" typically died while in a semiconscious condition of "long duration." Surviving animals often remained in a semi-conscious state of sedation and lethargy 4- to 6-hours post-exposure before showing signs of recovery. An LC50 value of 2770 ppm, LC05 value of 2489 ppm, and LC01 value of 2250 ppm were calculated by the method of Litchfield and Wilcoxon.

Four hour (male Swiss mice) LC_{50} = 2770 ppm

Benzene
Method approximates OECD Test Guideline, 403 but females only were tested. Groups of 10 female animals were exposed to benzene via inhalation for hour hours, then observed for 2 weeks following exposure. Animals dying during exposure and those killed at end of study subjected to necropsy. The LC50 value was reported as 13,700 ppm (converts to 44.7 mg/l) with 95% confidence limits of 13,050-14,480 ppm (converts 42.5 – 46.9 mg/l). Animals which survived the first 24 hours after exposure survived to the end of the 14 day observation period. Death appeared to be caused by a depression of the CNS. These animals had increased lung and liver weights, lung and liver congestion (increase in number of red blood cells and an increased number of vacuolated hepatocytes in the liver) (Drew and Fout, 1974).

Four hour (female Sprague-Dawley rat) LC50 = 13,700 ppm

1,3-Butadiene
Type: LC50
The four-hour LC_{50} in rats and two-hour LC_{50} in mice were determined in a non-guideline study. The objective of study was to determine hydrocarbon concentrations in various tissues at lethal exposure concentrations. Animals were not observed after exposure and no clinical observations were reported. The rat LC50 (4 hour) = 129,000 ppm with 95% confidence limits of 99,126-167,473 ppm. The mouse LC50 (2 hour) = 122,000 ppm with 95% confidence limits of 99,126-167,473 ppm (Shugaev, 1969)

Four hour (rat) LC50 = 129,000 ppm

C1 – C4 Hydrocarbons
The acute toxicity of 2-butene was evaluated in an OECD Limit Test in Wistar rats. Groups of five male and five females were exposed to 10,000 ppm (23.1 g/m^3) of 2-butene (racemic mixture: 95% purity, 42.4% *cis*, 55.3% *trans*)

or filtered air for four hours. Chamber concentrations were monitored by FID. Rats were then housed individually for 14 days of observation. Body weights were measured prior to exposure and on post-exposure days 7 and 14. Clinical signs were evaluated during exposure and daily thereafter. At day 14 animals were euthanized for macroscopic evaluation. No mortality was observed during the study. Restlessness was observed during and after exposure on the first day. No signs of clinical toxicity were observed for the remainder of the 14 day observation period. Body weights and gross pathology was comparable to control animals. The LC50 was greater than 10,000 ppm (Arts, 1992). In selecting 2-butene to represent the acute toxicity of the C1 – C4 HC fraction, the entire C1-C4 HC fraction concentration is assumed to be 100% 2-butene for purposes of calculating C1 – C4 HC acute toxicity ranges for each refinery gas.

Four hour (male and female Wistar rat) LC50 > 10,000 ppm (highest dose tested)

C5 – C6 Light End Naphtha Hydrocarbons

Light alkylate naphtha (API 83-19; CAS #64741-66-8; approx 100% paraffinic) is not acutely toxic. A group of 5 male and 5 female rats were exposed by whole body inhalation to API 83-19 at a nominal concentration of 5mg/l for 4 hours. This was achieved by total volatilization of the test material and appropriate dilution with air. After the 4 hour exposure the rats were observed twice daily for mortality. The animals were weighed prior to exposure and again on days 7 and 14 post exposure. On day 14 all surviving animals were killed by exsanguination following sodium pentobarbital anesthesia. For all animals, including those found dead during the study the lungs were removed, fixed and examined histologically. The mean analytical and nominal exposure concentrations were 5.04 ± 0.74 and 6.31 mg/l respectively. All animals survived the study but exhibited languid behavior and a hunched appearance during the exposure. Female body weights were decreased at day 15 but this was attributed to pre-necropsy fasting. At necropsy there were no remarkable findings and histopathology of the lungs was normal (API, 1987a).

Light catalytic cracked naphtha (API 83-20; CAS #64741-55-5, approx. 46% olefinic) is not acutely toxic. A group of 5 male and 5 female rats were exposed by whole body inhalation to API 83-20 at a nominal concentration of 5mg/l for 4 hours. After the 4 hour exposure the rats were observed twice daily for mortality. The animals were weighed prior to exposure and again on days 7 and 14 post exposure. On day 14 all surviving animals were killed and subjected to a gross post-mortem examination. For all animals, including those found dead during the study, the lungs were removed, fixed and examined histologically The mean analytical exposure concentration was measured and found to be 5.28 ±0.55 mgL. Gravimetric samples, collected on glass fiber filters suggested little or no aerosol in the chamber. Most animals exhibited languid behavior and squinted eyes during the second hour of the exposure. Polypnea was observed in all animals when removed from the chamber at the one hour post exposure observation period. Rhinorrhea was exhibited by two animals on day two of the test. All animals appeared normal subsequently and there were no mortalities during the study. With the exception of one animal (female) all animals had body weights that were considered unremarkable. There were no remarkable gross or microscopic findings (API, 1987b).

Sweetened naphtha (API 81-08, CAS #64741-87-3, approx. 21% naphthenics) is not acutely toxic. A group of 5 male and 5 female rats were exposed by whole body inhalation to API 81-08 at a nominal concentration of 5mg/l for 4 hours. After the 4 hour exposure the rats were observed twice daily for mortality. The animals were weighed prior to exposure and again on days 7 and 14 post exposure. On day 14 all surviving animals were killed by exsanguination following sodium pentobarbital anesthesia and were subjected to a full necropsy. For all animals, including those found dead during the study the lungs were removed, fixed and examined histologically. The actual chamber concentrations were found to be 5.2 mg/l. No deaths occurred during the study. There were no unusual pharmacotoxic signs or behavior observed in the control animals. There was however, a slight incidence of nasal discharge (2/5 males and 1/5 females) during the exposure period but none during the following 14 day observation period. The body weight gains for the males exposed to API 81-08 was considered normal but the female body weight gains were marginally less than that of the controls on day 14 post exposure (8.2% compared to 13.8% increase over pre-exposure body weight). No significant macro or microscopic changes were observed that were considered to be treatment related (API, 1987c).

Full range catalytic reformed naphtha (API 83-05, CAS #68955-35-1, approx. 63% aromatics) is not acutely toxic. A group of 5 male and 5 female rats were exposed by whole body inhalation to API 83-05 at a nominal concentration of 5mg/l for 4 hours. After the 4 hour exposure the rats were observed twice daily for mortality. The animals were weighed prior to exposure and again on days 7 and 14 post exposure. On day 14 all surviving animals

were killed by exsanguination following methoxyflurane anesthesia and were subjected to a full necropsy. For all animals, including those found dead during the study the lungs were removed, fixed and examined histologically. The exposure chamber TWA concentration was determined to be 5.22 ± 0.14 mg/l. No animal died during the study and no clinical signs of systemic toxicity were observed. There were no significant gross observations at necropsy and no histological changes were observed in the lungs. The 4 hour LC_{50} was therefore greater than 5.22 mg/l (API, 1984).

Results of testing naphtha blending streams for acute toxicity indicate that these materials demonstrate consistently low toxicity by the inhalation [rat LC50 >5g/m^3] exposure route. Weight of the evidence indicates that the C5 – C6 light naphtha hydrocarbon inhalation acute toxicity LC50 is > 5g/m^3 (~1063 ppm).

Four hour (rat) LC_{50} > 1063 ppm

Acute Toxicity Conclusions

Acute toxicity LC50 values have been experimental developed for all of the inorganic constituents of refinery gases with the exception of the asphyxiant gases. No acute toxicity LC50 values have been derived for the C1 – C4 and C5 – C6 hydrocarbon fractions; no mortality was observed at the highest exposure levels tested for these refinery gas constituents. The order of acute toxicity of refinery gas constituents from most to least toxic is[4]:

Hydrogen sulfide (LC50 = 444 ppm) > methyl mercaptan (LC50 = 675 ppm) > C5 – C6 HCs (LC50 > 1063 ppm) >ammonia (LC50 ~ 1590 ppm) > carbon monoxide (LC50 = 1807 ppm) > ethyl mercaptan (LC50 = 2,770 ppm) > C1 – C4 HCs (LC50 > 10,000 ppm) > benzene (LC50 = 13,700 ppm) > butadiene (LC50 = 129,000 ppm) > asphyxiant gases (hydrogen, carbon dioxide, nitrogen)

7.2 Repeated-Dose Toxicity

Ammonia
The repeated dose toxicity of ammonia was evaluated in Wistar rats. Eight – 14 male rats per group were exposed to 0, 50 or 90 ppm ammonia continuously for 50 days. Clinical signs, body weight gain, food intake, haemoglobin, haematocrit, erythrocyte count, total and differential leucocyte count, total protein, lung- and liver weights. Bartlett's and Scheffe's statistical tests were used to analyze the data. There was no mortality in any of the group during the study. Clinical observations in treated rats were comparable to controls. Body weight gain was 105% and 95% of control values for 50 ppm and 90 ppm, respectively. Food intake was 94% and 108% of control values for 50 ppm and 90 ppm, respectively. There were no treatment-related effects on organ weights. Hemaglobin and hematocrit values were increased in the 90 ppm group. The LOAEL and NOAEL were 90 ppm and 50 ppm, respectively. (Stolpe and Sedlag R, 1976)
In evaluating the health effects of ammonia, it should be kept in mind that ammonia is an endogenous compound in humans and derived from normal metabolic processes. Mean values in healthy humans vary by age with means ranging from 54 – 38.5 μmol/L. The highest values are found in infants < 30 days of age (Diaz *et al*., 1995).

LOAEL (male Wistar rat) = 90 ppm
NOAEL (male Wistar rat) = 50 ppm

Carbon monoxide
In a study found in the older medical literature, normal monkeys and monkeys with induced myocardial infarction were continuously exposed to 100 ppm carbon monoxide for 24 weeks (23 hr/day) and the physiologic effects on the cardiovascular system were evaluated. The objective for a 3 or 6 months study in Cynomolgus monkeys *(Macaca irus irus)* was to determine the cardiovascular effects of continuous exposure to carbon monoxide. Fifty-two animals (no gender information given) were randomly selected assigned to an air group or carbon monoxide group.

[4] ranking is not precise since several values were the highest dose tested

Myocardial infarction was induced in 26 of these animals. Control (air) and treated animals were housed in their respective chambers for one week prior to initiation of the carbon monoxide exposure procedures so they could acclimatize to their surroundings. Two exposure periods were used. In the first experiment, the animals were continuously exposed to 100 ppm carbon monoxide (23 hr/day) for three months; in the second experiment, the exposure period was extended to six months. The animals were divided into four groups: group 1 consisted of normal, air breathing animals; group 2 consisted of infarcted, air breathing animals; group 3 consisted of normal animals exposed to carbon monoxide; and, group 4 consisted of infarcted animals exposed to carbon monoxide. In the three·month exposure groups there were six animals in each group, and in the six·month exposure groups there were seven animals per group. During the exposure period blood was drawn every three weeks from each animal for chemical analyses and hematology; ECGs and body temperature were also recorded. The general well-being of the animals was assessed daily (alertness, food and water intake, stools, respiration, body weight). At the conclusion of the exposure period the animals were killed; gross observations were made on the heart and other tissues (brain, liver, spleen, kidney, lung, muscle, adrenals, and specimens were obtained for microscopic study.

Histopathological changes consistent with those seen in human pathology following myocardial infarction were observed in the monkeys in which infarction was induced. Recognizable scarring and perivascular changes associated with the infarction occurred and significant and characteristic increases in the hematocrit, hemoglobin, and RBC levels were observed after three weeks exposure to 100 ppm carbon monoxide in both infarcted and non-infarcted animals. The changes persisted until the animals were killed three or six months later. The values of mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, mean corpuscular volume, platelets, blood cell count, fibrin split products, and serum enzymes (CPK, GOT, and LDH) did not change significantly during carbon monoxide inhalation. The ECGs of infarcted and noninfarcted animals breathing carbon monoxide displayed elevated P wave amplitudes. An analysis of variance of the P-wave amplitude changes (in millimeters) indicates that infarction was the source of significant variation during the early phase of the exposure period (ie, up to six weeks,$P < .025$ [F test]. By the 21st week of exposure the effect of infarction was minimal, presumably because healing was well advanced. Conversely, elevation of the P wave amplitude attributable to carbon monoxide inhalation was highly significant during the latter part of the exposure period (week 21, $P < 0.001$ [F test]). Of those animals which exhibited elevated P waves following exposure to carbon monoxide, four were randomly selected for histologic examination of the atria. Marked nuclear hyperplasia was observed in three, and minimal hyperplasia was seen in one, suggesting atrial hypertrophy. There was no pathological evidence of carbon monoxide-related changes in other tissues examined (i.e., brain, spleen, muscle, lung, kidney, adrenal). The study LOAEL ≤ 100 ppm, the only dose tested. (DeBias *et al*., 1973).

LOAEL (Cynomolgus monkeys *(Macaca irus irus)* **≤ 100 ppm (lowest dose tested)**

Hydrogen sulfide
A 90-day inhalation toxicity study using Fisher 344 rats, Sprague Dawley rats, and B6C3Fl mice (exposed simultaneously in the same chamber) was conducted with H2S vapor. The study was conducted according to OECD guideline 413. Three groups per species/strain (15 male/15 female per group) were exposed to atmospheres of 10, 30, or 80 ppm hydrogen sulfide, respectively. In addition, control groups (15 male/15 female) were exposed to clean air only and were handled in a similar manner to that of the test animals. The duration of exposure was 6hrs/day, 5days/wk, for at least 90 days. There was also a 10-day post exposure observation period. There was no mortality during the 90 day study. Clinical observations included crustiness associated with the animal's ear tag, crusty nose, eyes and muzzle, lacrimation, rales, yellow/brown stained fur and red stained fur. A significant decrease in body weight gains of all treatment groups of both sexes was noted after the first week of exposure. Body weights of the treated groups continued to lag behind the control group over the next 12 weeks. No significant changes were noted with respect to food consumption, opthalmology, neurological function, clinical pathology, and organ weight data. Gross and histopathologic studies did not reveal any lesions attributable to test article exposure in the rats. Inflammation of the nasal mucosa described as minimal to mild rhinitis was observed in the B6C3Fl mice highest dose (80 ppm) group. Special neuropathological studies preformed on teased fibers from muscular and neural branches of the tibial nerve, together with Epon embedded specimens from cervical and lumber spinal cord from control and high dose animals did not show neuropathologic changes (CIIT 1983 a,b,c).

In the original rat study report, no respiratory effects were noted in the rats and inflammation of the nasal mucosa described as minimal to mild rhinitis was observed in the B6C3Fl mice highest dose (80 ppm) group. However, a histological re-examination of the study slides revealed significant increases in incidence of olfactory neuronal loss in Sprague-Dawley and female F-344 rats at 30 and 80 ppm, and in Sprague-Dawley male rats exposed to 80 ppm. Increases in bronchiolar epithelial hypertrophy and hyperplasia were also reported in female Sprague-Dawley rats at 30 and 80 ppm hydrogen sulfide and male rats of both strains at 80 ppm. Increases in bronchiolar epithelial hypertrophy and hyperplasia were not observed in female F-344. The No Observable Adverse Effects Levels (NOAEL) for male & female Sprague-Dawley rats and female F-344 rats were 10 ppm, and 30 ppm for male F-344 rats (based on olfactory neuron loss). The re-examination of the slides from the B6C3Fl mice confirmed the initial results and also reported significant increases in olfactory neuron loss at 30 and 80 ppm. The mouse LOAEL was 30 ppm and the NOAEL was 10 ppm (Doorman *et al.*, 2004). These results confirmed similar results seen previously in male Sprague-Dawley rats exposed to hydrogen sulfide for 6 hr/day, 7 days/week for 10 weeks (Brenneman *et al.*, 2000).

NOAEL (male & female Sprague-Dawley rats and female F-344 rats) = 10 ppm
NOAEL (male F-344 rat) = 30 ppm
NOAEL (male and female B6C3Fl mice) = 10 ppm

Methanethiol
Groups of male Sprague-Dawley rats (3l/group) were exposed whole-body to concentrations of 0, 2, 17 or 57 ppm methyl mercaptan, 7 hrs/day, 5 days/week for 3 months. A subset of 10 animals from each group was designated for special metabolic performance studies. At the end of the exposures the metabolic subset animals were placed overnight in metabolism cages and the appropriate measurements were made. Metabolic performance measurements were made for 17 h periods on 5 consecutive days. At the end of the 3-mo experimental period the metabolic subset animals served as the subjects for the following tests: intestinal transit time, systolic blood pressure effects, and histological examination of selected organs (heart, lungs, small intestine, liver, and kidneys). The observations were made at least 24 h later than the end of the last exposure day. Data obtained from the remaining 21 animals per group included terminal body weight, 0_2 consumption, SMA 12160 blood analyses, organ weights (brain, lung, liver, spleen, heart, kidneys, and adrenals), and liver histopathological evaluation.

No mortality was observed in contol and treated groups during the 3-mo period. There was an observation of rats huddling in groups toward the periphery of the chamber with noses pointed outward from the chamber's vertical axis in the high exposure (57 ppm) group. There was a statistically significant dose-related trend toward decreased terminal body weights that reached the level of statistical significance in the regular and metabolic subset of animals at the highest exposure (57 ppm). The average weights of a few organs were significantly different from corresponding control values with no obvious dose-related trend; these differences were not considered to be treatment related. Statistically significant changes were observed sporatically in clinical chemistry from treated animals of all exposed groups. The parameters affected in one or more treated groups were total serum proteins (increased), albumin (decreased), inorganic phosphate (decreased), cholesterol (increased), bilirubin (increased), blood urea nitrogen (decreased), and lactate dehydrogenase (decreased). None of these trends were dose-related at the 95% confidence level.No significant differences were observed in any of the metabolic parameters assessed.

There were no differences between control and treated groups in histological evaluation of lungs heart, small bowel, and kidneys, although it was noted that lung observations included pneumonia, empysematic changes, and occational fibrosis described as “characteristic of rat colonies”. Some evidence of mild inflammatory cell infiltration in the absence of inflammation was observed in the liver, along with “possibly” enlarged bile ductules (all treatment groups). One hepatic carcinoma was observed in the 17 ppm group. Based on decreased body weight, the study LOAEL = 57 ppm and the NOAEL = 17 ppm (Tansy et al., 1981).

LOAEL (male Sprague Dawley rats) = 57 ppm
NOAEL (male Sprague Dawley rats) = 17 ppm

Ethanthiol

No suitable subchronic study for ethanethiol was available. Subchronic toxicity will be assumed to be the same as that of methanethiol (read across from methanethiol); see study summary immediately above.

LOAEL (male Sprague Dawley rats) = 57 ppm
NOAEL (male Sprague Dawley rats) = 17 ppm

Benzene
Male CD-1 mice (11–12/group) were exposed for 6 hours/day, 5 days/week to concentrations of 0 or 10 ppm (0 or 32 mg/m^3) benzene for 10 weeks or to 0 or 300 ppm (0 or 958 mg/m^3) for 26 weeks (Green et al., 1981a,b). On the day of the last exposure, samples (pooled from groups of 3–4 mice) were obtained from the peripheral blood, bone marrow, and spleen to evaluate hematologic and hematopoietic cells. In mice exposed to 10 ppm (32 mg/m^3), no adverse effects were observed with respect to mortality, body weight, or cells in the peripheral blood or bone marrow. Spleen weight, total nucleated cells per spleen, and nucleated RBCs per spleen were significantly increased ($p<0.05$) in mice exposed to 10 ppm (32 mg/m^3). Mice exposed to 300 ppm (958 mg/m^3) had the following significant ($p<0.05$) changes: increased mortality rate; decreased numbers of lymphocytes and RBCs in peripheral blood; decreased granulocyte/macrophage progenitor cells in bone marrow; decreased spleen weight and numbers of lymphocytes; multipotential hematopoietic stem cells and committed granulocyte/macrophage progenitor cells in the spleen; and increased incidence of atypical cell morphology in the peripheral blood, bone marrow, and spleen. These studies identify a LOAEL ≤ 10 ppm (32 mg/m^3) for slight hematopoietic effects in mice exposed to benzene for 10 weeks.

LOAEL (mice) ≤ 10 ppm (lowest dose tested)

1,3-Butadiene
In considering the toxicity of 1,3-butadiene, it is important to determine the appropriate animal model for use in hazard characterization. It is generally agreed that butadiene produces toxicity when it is metabolized to its reactive metabolites after animals are exposed to butadiene. However, there are differences in metabolism amongst species. The basis of the species differences between rats and mice may be related to the greater production of toxic intermediates and a lower capacity for detoxification of these intermediates (USEPA 2002a). The metabolism of 1,3-butadiene and the toxicity of its reactive epoxide metabolites has been well studied. 1,3-Butadiene is first metabolized to 1,2-epoxy-3-butene (EB), a process that is primarily associated with cytochrome P450 (CYP) 2E1, but can also be accomplished by additional isoforms including CYP 2A6 and 4B1. This electrophilic metabolite can be detoxified by conjugation with glutathione and subsequent excretion in the urine as urinary metabolites 1-hydroxy-2-(N-acetylcysteinyl)-3-butene and 2-hydroxy-1-(N-acetylcysteinyl)-3-butene (collectively known as M2 metabolite). It can also undergo hydrolysis by epoxide hydrolase (EH) to form 3-butene-1,2-diol (butene-diol). Butene-diol can also be conjugated with glutathione and subsequently excreted in the urine as urinary 1,2-dihydroxy-4-(N-acetylcysteinly)-butane (M1 metabolite). It can be further oxidized by cytochrome P450 to the 1,2-dihydroxy-3,4-epoxybutane (EBD). An alternative pathway for the metabolism of EB is oxidation to the 1,2:3,4-diepoxybutane (DEB) which can be further hydrolyzed to EBD or conjugated by glutathione. This series of epoxidation and detoxication steps generates three electrophilic metabolites: EB, DEB, and EBD (Himmelstein *et al.*, 1997; TCEQ, 2008). *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). The second oxidation step to DEB could be mediated *in vitro* only by mouse liver microsomes (Csanady *et al.*, 1992). Cochrane and Skopek (1994) have shown that DEB is 100 times more mutagenic than EB and 200 times more mutagenic than EBD in human lymphocytes. The extent to which DEB is produced and reaches target tissues will play a role in the toxicity (Kligerman and Yu 2007). Mice form more DEB than rats or humans whereas EBD is more readily formed in humans than in rats (Slikker *et al.* 2004; Swenberg *et al.* 2007). *In vivo* studies of 1,3-butadiene metabolism in mice and rats have also shown large interspecies differences. M1/(M1 + M2) metabolite 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 (TCEQ, 2008). The existing metabolism data suggest that metabolism in humans appears to be more like metabolism in rats than in mice (ACC, 2004). Based upon this brief summary, and the more detailed information referenced, rat data will be used to

estimate the 1,3-butadiene component for toxicities associated with Refinery Gases Category Member repeated-dose, developmental, and reproductive hazards.

Three groups (110 male/110 female per group) of Sprague-Dawley rats were chamber-exposed to atmospheres of 0, 1000, and 8000 ppm 1,3-butadiene for two years. Control groups were exposed to clean air only. At 52 weeks, 10 males and 10 females from all groups were killed. The remainding animals were sacrificed when survival was approximately 20-25% (105 weeks for females and 111 weeks for males). The exposure was 6 hrs/day, 5days/wk. All animals were observed twice daily, before and after exposure, and a detailed observation was performed at weekly intervals. Individual body weights were recorded weekly up to week 13, then every 2 weeks to week 52 and monthly thereafter. Clinical chemistries, neuromuscular function and detailed post-mortem examinations were performed at the time of sacrifice. Analysis of the survival data, subcutaneous masses, lesions/tumor incidences was performed using a variety of statistical methods; body weights, laboratory investigations, and organs weights were analyzed by using analysis of variance and Student's t-test.

Clinical signs that appeared to be related to treatment were seen in the second until the fifth month of exposure. Minor, treatment-related clinical signs of toxicity – wet and ruffled fur together with slight limb weakness or incoordination following dosing on the first day of the 5-day schedule – were seen between 2 and 5 months of treatment in animals at 8000 ppm. There were no effects on hematology, blood chemistry, urine analysis, and neuromuscular function that could be associated with treatment with 1,3-butadiene. Changes in clinical condition, suppression of body weight gain, reduced survival and increases in certain organ weights and in both common and uncommon tumor types occurred at 8000 ppm. At 8000 ppm, males had statistically significantly increased kidney, heart, lung and spleen weights, with associated nephrosis of the kidney and focal metaplasia in the lung. At the end of the study, statistically significant increases were seen in liver weight in all exposure groups, but there was no associated pathology. For both sexes, the LOAEL = 8000 ppm and the NOAEL = 1000 ppm (Owen and Glaister, 1990).

LOAEL (male and female Sprague Dawley rats) = 8,000 ppm
NOAEL (male and female Sprague Dawley rats) = 1,000 ppm

C1 – C4 Hydrocarbons
The repeated dose toxicity of a racemic mixture of 2-butene (cis and trans, 95% purity) was assessed an OECD 422 Combined Repeated Dose Toxicitywith the Reproductive/Developmental Toxicity Screening Test. Twelve male and 12 female Wistar rats per group were exposed to 0, 2500 or 5000 ppm 2-butene for 6 hours/day, 7 days/week. Males were exposed for 39 to 46 days; females were exposed two weeks prior to mating, through mating, and to gestation day 19. Body weights and food consumption were recorded. At study termination, hematology and clinical chemistries were conducted on blood, gross necropsies were conducted, organs weights were recorded and tissues processed for microscopic evaluation. Control and high dose groups, only, were evaluated microscopically. Body weight change was lower for male rats in the first and fourth weeks of exposure in the 2500 ppm group and in the first week in the 5000 ppm group. Female body weights were reduced in the 2500 ppm group at 14 days of exposure and the 5000 ppm group at 7 and 14 days of exposure. Female body weights were comparable during mating and gestation, but were reduced in the 5000 ppm group on lactation day 1. Male rats in both exposure groups had increased total white cell and lymphocyte counts, however there was no dose-response and counts were within historical control range. A decrease in plasma calcium concentration was observed in high dose males. No other adverse treatment related effected were observed. The repeated-dose NOAEL for both sexes was 2500 ppm. The repeated-dose LOAEL for both sexes was 5000 ppm (Waalkens-Grendsen and Arts, 1992). In selecting 2-butene to represent the repeated-dose toxicity of the C1 – C4 HC fraction, the entire C1-C4 HC fraction concentration in each refinery gas is assumed to be 100% 2-butene for purposes of calculating C1 – C4 HC repeated-dose toxicity ranges for each refinery gas.

LOAEL (male and female Wistar rat repeat dose) = 5000 ppm
NOAEL (male and female Wistar rat repeat dose) = 2500 ppm

C5 – C6 Light End Naphtha Hydrocarbons
Baseline Gasoline Vapor Condensate [BGVC], a 20% light fraction of a whole unleaded gasoline sample was evaluated in a 13- week inhalation study according to OPPTS 870.3465. This test material was a representative evaporative emission tested under the USEPA 211(b) Fuels and Fuel Additives Health Effects Testing Program (1994b, 1998). BGVC was administered to Sprague Dawley rats (10/sex/group) at target concentrations of 0, 2000, 10000, and 20000mg/m^3 (actual concentrations 0, 2050, 10,153 and 20,324 mg/m^3) 6hr/day, 5 days/week for 13 weeks. Additional groups of control and high dose rats (10/sex/group) were also exposed and retained untreated for an additional 4- week recovery period (API, 2005a). Clinical signs, body weights and body weight changes, and food consumption were recorded throughout the study. Opthalmoscopic evaluations were performed pretest and at exposure termination. Hematology, coagulation and clinical chemistry parameters were measured at week 4 and week 13. Neurobehavior evaluation of motor activity and functional activity [FOB] were performed on 10 rats/sex/group pretest and during weeks 3, 7, and 12 of exposure according to OPPTS 870.6200. After 13 weeks exposure rats were sacrificed except for recovery animals sacrificed 4 weeks later. Fourteen selected organs were weighed. Histopathology examination was performed on 31 tissues from rats in the control and high dose groups and on kidneys from rats in all groups. Five rats/sex/group were perfused for neuropathology and sections of brain, eye, spinal cord, peripheral nerves and ganglia were examined microscopically. Satellite groups of animals were exposed to BGVC with the subchronic rats for immunotoxicology, genetic toxicity and glial fibrillary acidic protein (GFAP) analyses. The genetic toxicology studies are presented in Section 7.1.4 of this document. The immunotoxicology and GFAP report details are provided in robust summaries, and are not considered further here other than to state that BGVC did not produce significant effects in the parameters measured in these two satellite studies.

Test animals were generally unremarkable in exposure chambers and during non-exposure periods except for a slight increase in red nasal discharge seen in 20,324mg/m^3 animals during 13 weeks of exposure but not during recovery. No adverse effects were induced by BGVC on ophthalmology, body weights, feed consumption or blood chemistry parameters. No toxicologically significant changes were observed in organ weights although male absolute and relative kidney weights were slightly elevated at the mid and high dose levels. Gross abnormalities were not seen at terminal sacrifice. Dose related microscopic findings included eosinophilic material in the nasolacrimal ducts in high dose rats consistent with reported red nasal discharge and renal histopathologic changes in kidneys of all treated male rats. These renal changes were consistent with alpha 2-microglobulin mediated nephropathy, a species and sex-specific change not considered relevant to human health (USEPA, 1991). Kidneys of recovery 20,324mg/m^3 male rats had nearly complete resolution of these changes. BGVC did not cause adverse neurobehavioral or neuropathologic effects. The systemic LOAEL [excluding male kidney effects] = 2,0324mg/m^3 (~ 6,625 ppm) and NOAEL = 10,153mg/m^3 (~ 3,310 ppm). NOAEL for neurotoxicology = 20,324mg/m^3 (~ 6,625 ppm). (API, 2005a).

LOAEL (male and female Sprague Dawley rats) = 6,625 ppm
NOAEL (male and female Sprague Dawley rats) = 3,310 ppm

Repeated-Dose Conclusions

With the exception of the asphyxiant gases, repeated dose toxicity has been observed in all individual refinery gas constituents. With the exception of benzene and the asphyxiant gases, the repeated-dose effects of inorganic components of Refinery Gases are produced at lower concentrations than are those produced by the hydrocarbon components. Based upon LOAEL values, the order of order of repeated-does toxicity of these constituents from most toxic to the least toxic is:

Benzene (LOAEL ≤ 10 ppm) < Hydrogen sulfide (LOAEL = 30 ppm) > methyl mercaptan (LOAEL = 57 ppm) = ethyl mercaptan (LOAEL = 57 ppm) >ammonia (LOAEL = 90 ppm) > carbon monoxide (LOAEL ≤ 120 ppm) >C1 – C4 HCs (LOAEL = 5,000 ppm; assumed to be 100% 2-butene) > C5 – C6 HCs (LOAEL = 6,625 ppm) > butadiene (LOAEL = 8,000 ppm) > asphyxiant gases (hydrogen, carbon dioxide, nitrogen)

7.3 In Vitro Genetic Toxicity

Ammonia[5]
Ammonia was tested in a bacterial mutation assay in *Salmonella typhimurium* and *Escherichia coli* with and without metabolic activation from a KC500 polychorinated biphenyl-induced rat liver homogenate mixture. Salmonella strains TA98, TA100, TA1535, TA1537, and TA1538 and *E. coli* strain WP2uvrA were tested in duplicate. Agar plates without lids were exposed for 48 hours to 0, 500, 1000, 2500, 10000 or 25000 ppm ammonia. The appropriate concurrent positive and negative controls were used. No mutagenic activity was observed in any bacterial strain at any concentration. Ammonia was not a mutagen with and without metabolic activation in this test system (Shimizu *et al.* 1985).

Negative for *in vitro* bacterial mutagenicity

No data for *in vitro* non-bacterial genotoxicity

Carbon monoxide
No *in vitro* genotoxicity data available.

Hydrogen sulfide
Hydrogen sulfide gas was evaluated in a standard bacterial assay using *Salmonella typhimurium* TA97, TA98, and TA100 strains with or without metabolic activation. Metabolic activation was provided by S9 liver fractions of male Syrian golden hamsters or Sprague-Dawley rats that had been induced with 500 mg/kg Aroclor 1254. The concentrations tested were 17, 57, 175, 582 and 1750 μg/plate. The concentration of hydrogen sulfide gas was limited to 1750 μg/plate by its solubility in the test solvent ethanol. Appropriate positive and solvent controls were evaluated concurrently with test samples. The criterion for a positive test was a mutant frequency greater than or equal to twice the negative control frequency. Hydrogen sulfide was not mutagenic in any strain tested with or without metabolic activation (USEPA 1984).

Negative for *in vitro* bacterial mutagenicity

There are no *in vitro* chromosomal aberration data available for hydrogen sulfide. Read across data from mercaptans (Methanethiol, sodium salt) is appropriate for this endpoint (MTC, 2001).

Equivocal for *in vitro* non-bacterial genotoxicity

Methanethiol
There are no in vitro genotoxicity studies available for the methanethiol. The toxicity value for bacterial mutagenicity and chromosomal aberrations will be read across from methanethiol, sodium salt (MTC, 2001).

Negative for bacterial mutagenicity
Equivocal for *in vitro* non-bacterial genotoxicity

Ethanethiol
Ethanethiol was evaluated in a standard bacterial assay using *Salmonella typhimurium* TA98, TA100, TA1535, TA1537, and TA1538 strains, with or without metabolic activation. Metabolic activation was provided by S9 liver fractions from Aroclor 1254-induced rats. The test material was tested in triplicate at 0, 124, 370, 1111, 3333, and 10,000 μg/plate. Appropriate positive and solvent controls were evaluated concurrently with test samples. The criteria for a positive test were a mutant frequency greater than or equal to twice the negative control frequency. The

[5] The 2004 ATSDR Ammonia Toxicological profile (http://www.atsdr.cdc.gov/toxprofiles/tp126.html) concludes that "Taken together [i.e. weight of evidence], the data indicate that ammonia and ammonium ion may have clastogenic and mutagenic properties." However, ATSDR reports only one bacterial study (Dererec et al., 1951; not reported here) that used ammonia (NH_3) where positive activity was only observed at toxic doses causing 98% lethality.

cytotoxic concentration was 10,000 μg/plate. Ethanethiol was not mutagenic in any strain tested with or without metabolic activation (Hazleton Laboratories, 1984a).

Negative for bacterial mutagenicity

Ethyl mercaptan was tested in a Sister Chromatid Exchange (SCE) assay in Chinese Hamster Ovary (CHO) cells with or without metabolic activation system. Induction of SCEs is not a genotoxic event, per se, since no genetic material is lost and gene pairing of alleles remains intact. However, it does indicate an interaction with the DNA, which may or may not be confirmed as genotoxic in assays specifically designed to test for genotoxicity. Metabolic activation was provided by rat liver microsomal fraction (S9) of rats induced with Aroclor 1254. The test material was tested in triplicate at 0, 25, 84, 250, 840, and 2,500 μg/ml. Appropriate positive and solvent controls were evaluated concurrently with test samples. The cytotoxic concentration was 2,500 μg/plate. In the first test, all cells recovered at 2,500 μg/l were first division metaphases which could not be analyzed for SCE's. A repeat test was peformed with 2,500 μg/ml in which the chromosomes were recovered 43 hrs after exposure (instead of 24 hrs) in order to allow for two cell divisions. The criteria for a positive test were an SCE frequency greater than or equal to twice the negative control frequency. In the absence of S9 mix, an increase of SCEs was observed at 840 μg/ml, the second highest concentration of ethyl mercaptan, however the 2,500 μg/plate group could not be evaluated due to cytotoxicity. To overcome the cytotoxicity at 24 hours, a second test was conducted at the 2,500 μg/ml level and cells were allowed to grow for 43 hours before harvest. A statistically significant increase in SCE's was seen in the second test at 2,500 μg/ml both with and without metabolic activation, and a greater than two-fold increase in SCE's was seen both with and without activation. Ethyl mercaptan is positive for inducing SCEs in cultured CHO cells with and without a metabolic activation system (Hazleton Laboratories, 1984b).

Positive for induction of non-bacterial chromosomal SCEs

Methanethiol, sodium salt
Methanethiol, sodium salt is a supplemental compound for in vitro mutagenicity in support of methanethiol and hydrogen sulfide. The two mutagenicity studies presented below are the only data provided for methanethiol, sodium salt.

The *in vitro* potential mutagenic activity of sodium methanethiol was investigated in a standard bacterial test with and without metabolic activation (microsomal fraction S9 of rats treated with Aroclor 1254) in 5 strains of bacteria *Salmonella typhimurium*: TA 1535, TA 1537, TA 102, TA 98 and TA 100. Test concentrations were 312.5, 625, 1250, 2500 and 5000 μg/plate, except in the second test for the TA 98 and TA 102 strains without S9 mix: 1.25, 250, 500, 1000 and 2000 μg/plate, and for the TA 102 strain with S9 mix: 312.5, 625, 1250, 2500 and 4000 μg/plate. The test substance was not mutagenic with or without metabolic activation (ELF ATOCHEM, 1992).

Negative for *in vitro* bacterial mutagenicity

Methanethiol, sodium salt was tested in an OECD guideline 473 *in vitro* mammalian chromosomal aberration test with and without metabolic activation from Aroclor 1254 induced rat liver microsomes. Concentrations tested were 30, 60, 90, 120, 240, 480 μg//ml. Sodium methylmercaptide did not induce structural chromosome aberrations both with and without S9 mix for both harvests. However, without S9 mix an increase in the number of polyploid cells was recorded at the 44-hour harvest at 90 and 120 μg/ml (4.0% and 14.5% respectively vs. 0%). Therefore, a complementary test without S9 mix at the 44-hour harvest was performed using the following doses: 50, 100 and 150 μg/ml. Since the mitotic index was reduced by more than 90% at 150 μg/ml, only slides from the 50 and 100 μg/ml treatment-level were scored. Three % polyploidy was noted at 100 μg/ml and 0% at 50 μg/ml. The frequencies of cells with structural chromosome aberrations of the vehicle and positive controls were as specified in acceptance criteria and within the range of the historical data for both tests and both harvest times. See robust study summary document for a table of aberration frequencies. The potential for methanethiol, sodium salt to induce chromosomal aberrations was determined to be equivocal (ELF ATOCHEM, 1995).

Equivocal for *in vitro* non-bacterial genotoxicity

Benzene

The *in vitro* potential mutagenic activity of benzene was investigated by the Ames test using 4 strains of bacteria *Salmonella typhimurium*: TA 1535, TA 100, TA 104 and TA 98. This test enables the detection of base-pair substitution and frameshift mutagens. Tests were also conducted on benzene and its following metabolites (additional bacterial strains were added, i.e., TA 102 and TA 97): benzene oxide, phenol, hydroquinone, 4,4'-dihydroxybiphenyl, 2,2'-dihydroxy-biphenyl, quinone, trans-benzene-1,2-dihydrodiol , catechol and 1,2,4-trihydroxybenzene. Duroquinone, and anti-benzene-diol-epoxide, syn-benzene-diol-epoxide and 1,2,3-trihydroxybenzene were also included. *S. typhimurium* was exposed to benzene vapor in desiccators to allow for longer exposure periods (as opposed to plate incorporation method). The exposure atmospheric concentrations were 0, 3, 6, 15, 30, 100, 150, 300, 1000 ppm. Each assay was carried out both in the absence and in the presence of a metabolic activation system, NADPH-fortified, S9 mix derived from Aroclor 1254 induced rat or mouse liver homogenate (17 mg/plate). The test compound, bacteria and S9 fractions or buffer were preincubated for 20 min at 37°C and then added to minimal agar plates. After incubation for 3 days, the colonies were counted. A response was considered to be positive response if the number of colonies was > 2 times the control value. A cytotoxic concentration was not identified. Benzene was found to be mutagenic in the presence but not the absence of S9. The most responsive strain was TA 1535. A 2-fold increase in the number of mutants above control was observed even at a benzene concentration as low as 10 ppm. However, further increases in the concentration had only a modest effect. The maximal mutant number was about 3-fold the values for the control plates. Similar effects were then seen over a wide concentration range. In this same strain (TA 1535), the metabolites trans-benzene-1,2-dihydrodiol in the presence of S9 and anti-benzene-diol-epoxide and syn-benzene-diol-epoxide in the absence of S9 induced mutations. No other metabolite including catechol to which trans-benzene-1,2-dihydrodiol is converted by cytosolic dihydrodiol dehydrogenase, gave a positive result in strain TA1535. Mutagenic responses, some of them weak, were noted in other strains treated with 1,2,3-trihydroxybenzene, 1,2,4-trihydroxybenzene, catechol, quinine, hydroquinone, syn-benzene-diol-epoxide and anti-benzene-diol-epoxide. Benzene vapor was mutagenic in *S. typhimurium* TA 1535 in the presence but not the absence of S9 (Glatt *et al.*, 1989).

Positive for bacterial mutagenicity

Benzene was tested in a Sister Chromatid E (SCE) xchange assay in human peripheral lymocytes with or without metabolic activation system. Induction of SCEs is not a genotoxic event, per se, since no genetic material is lost and gene pairing of alleles remains intact. However, it does indicate an interaction with the DNA, which may or may not be confirmed as genotoxic in assays specifically designed to test for genotoxicity. Metabolic activation was provided by rat liver microsomal fraction (S9) of rats induced with Aroclor 1254. The test material was tested at 0, 16, 78, and 391 mg/L. Heparinized whole blood was obtained from healthy adult men. Benzene was dissolved in serum-free culture medium and the metabolic activation system (S9 mix derived from Aroclor-induced rat liver) and incubated in a flask for 2 hours. The flask was agitated to ensure even distribution of active metabolites among the cells. After incubation, the cells were washed, resuspended in the same medium and incubated further. SCEs were analyzed in 35 consecutive second-division cells for each point. 200 metaphase cells were scored to determine the percentage of cells in X1, X2, and X3+ divisions. An increased number of SCEs were found in cultures treated in the presence of 10% S9 mix. In the absence of S9 and at S9 concentrations of 1 or 90% no increase in the frequency of SCEs was noted. Ten % S9 mix was the optimal concentration for the induction of SCEs. When the cells were exposed to benzene concentrations of 2 X 10-4, 1X 10-3 and 5 X 10-3M (approximately 16, 78 and 391 mg/L), a dose-related increase in SCEs was seen when the appropriate activation concentration was used. It was hypothesized that S9 mix at 10-30% converted benzene into active forms that were cytotoxic and delayed cell turnover times. Further examination suggested that the metabolites responsible for cell division delay may be different from those which induce SCE. The addition of glutathione to the culture caused a dose-dependent decrease in SCEs in cells exposed to benzene and S9 mix. The addition of glutathione also completely prevented the induction of SCEs by catechol and hydroquinone, two major phenolic metabolites of benzene and potent inducers of SCEs. Benzene induced SCEs in a dose-dependent manner the presence but not the absence of the optimal amount of S9 (Morimoto, 1983).

Positive for induction of non-bacterial chromosomal SCEs

1,3-Butadiene
The *in vitro* potential mutagenic activity of 1,3-butadiene vapor was investigated in a bacterial mutagenicity assay using 4 strains of bacteria *Salmonella typhimurium*: TA97, TA98, TA100, and TA1535. This test enables the detection of base-pair substitution and frameshift mutagens. The test substance was tested in two independent assays. Each assay was carried out both in the absence and in the presence of a metabolic activation system (Arochlor 1254-induced and uninduced rat and mouse S9, and human S9) at a level of 0.8 mg/ protein/plate. Test material concentrations were 0, 30, 40, 50, and 60% 1,3-butadiene in air. Concentrations of 1,3-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. 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. *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% 1,3-butadiene in air with induced and uninduced rat S9 and mouse S9 (uninduced). In general, 1,3-butadiene was a weak *in vitro* genotoxin (Arce, 1990).

Positive for bacterial mutagenicity

1,3- Butadiene (BD), and BD metabolites monoepoxybutene and diepoxybutane, were tested in a Sister Chromatid Exchange (SCE) assay in Chinese Hamster Ovary (CHO) cells with or without metabolic activation system. Induction of SCEs is not a genotoxic event, per se, since no genetic material is lost and gene pairing of alleles remains intact. However, it does indicate an interaction with the DNA, which may or may not be confirmed as genotoxic in assays specifically designed to test for genotoxicity. Metabolic activation was provided by rat liver microsomal fraction (S9) of rats induced with Aroclor 1254. Appropriate positive and solvent controls were evaluated concurrently with test samples. The test chemicals were added after 24 hr of incubation, and then pulse treated. The duration of the pulse treatment was 4 hr in serum-free bromodeoxyuridine (BudR)-free medium, in the presence or absence of S9 mix. The cultures were rinsed and incubated for the next 24 hr with BudR added. The concentrations of chemicals, used in experiments were as follows: 1,3-butadiene, 25, 50, 100 and 200 μM; monoepoxybutene, 1, 5, 25, 50, 100 and 200 μM; diepoxybutane, 0.1, 1, 50 and 100 μM. Duplicate cultures were set up for each treatment. SCEs were stained and scored from the second-division cells. 60 cells per treatment point were analyzed and the statistical significances were calculated using a one-tailed Student's t-test. The cytotoxic concentrations of test material were >200 μM with and without metabolic activation. In the absence of S9 mix no increase of SCEs was observed even at the highest concentration of 1.3-butadiene. In the presence of S9, a slight dose response was observed. Both metabolites of 1.3-butadiene (monoepoxybutene and diepoxybutane) demonstrated a very clear dose-dependent increase in SCEs, both with and without S9 mix. 1,3-Butadiene is weakly positive for inducing SCEs in cultured CHO cells with a metabolic activation system (Sasiadek *et al.*, 1991).

Positive for induction of non-bacterial chromosomal SCEs

C1 – C4 Hydrocarbons
Hydrocarbons in the C1 – C4 range were not mutagenic in several *in vitro* bacterial cell test systems. C1 – C4 hydrocarbons that have been tested include methane, n-propane, n-butane, isobutane, liquefied petroleum gas (primarily butane and propane), ethylene, propylene, butylene, isobulyene and acetylene. Please see Appendix 4 for experimental systems and references. A study on 2-butene was selected for the C1 – C4 hydrocarbon bacterial mutagenicity key study.

The *in vitro* potential mutagenic activity of 2-butene (mixed isomers; 42.4% cis, 55.3% trans) was evaluated in an OECD Guideline #471 bacterial mutagenicity assay using 4 strains of *Salmonella typhimurium*: TA 1535, TA 1537,

TA 100, and TA 98. Activation system: Sprague Dawley male rat liver (S9 fraction). 10% S9 fraction in S9 mix, (0.05 ml S9 fraction/plate) Aroclor 1254 induced; 500mg/kg single ip injection 5 days before sacrifice. A 0.1 ml aliquot of *Salmonella*, 2.0 ml molten top agar, 0.5 ml S9 mix or 0.5 ml pH 7.4 phosphate buffer were mixed in a test tube and poured on minimal agar plates (3 plates/ conc./± S9 mix). Atmospheres of varying concentrations (0.0, 10, 20, 40, 60, 80%) were generated by mixing 2-butene with clean dry air, using precalibrated gas flow meters as gas flow indicators. Mixtures passed into 10L stainless steel containers holding Salmonella plates with triple vented lids. Concentrations were selected based on a preliminary range finding test with TA100 ± S9; dose-related reduction in frequency of revertant colonies and reduced growth of background lawn observed at 80, 100%. Containers holding 3 stacks of 8 plates each were flushed with appropriate concentrations of 2-butene for 5 minutes to allow system to equilibrate; containers were incubated at 37 C^o for 48 hrs and numbers of revertant colonies counted. Analytical determinations were performed by GC on syringe samples of test atmospheres at the differing concentrations. Positive control compounds were: -S9, N-ethyl-N' nitro-N-nitrosoguanidine, 3 μg/plate for TA100, 5 μg/plate for TA1535; 9 amino acridine, 80 μg/plate for TA1537; 4-Nitroquinoline-1-oxide, 0.2 μg/plate for TA98; +S9, 2-aminoanthracene 2 μg/plate for TA1535; benzo(a)pyrene 5 μg/plate for all other strains. Vinyl chloride (50% concentration) was the gaseous positive control for all strains; negative control was clean dry air. The complete experiment was repeated using fresh bacterial cultures, test material and control solutions. Criteria for positive response were induction of dose-related and statistically significant increases in mutation rate in one or more strain of bacteria ± S9 in both experiments at subtoxic doses. Toxicity was exhibited in all strains at 80% butene-2. In experiment 2, slight toxicity also occurred at 60%. No significant increases in number of revertant colonies of any strain of bacteria were observed at any dose concentration ± S9. Controls performed appropriately. 2-Butene was not mutagenic in the *Salmonella typhimurium* assay with or without metabolic activation (Thompson, 1992).

Negative for *in vitro* bacterial mutagenicity

Hydrocarbons in the C1 – C4 range are not mutagenic in several *in vitro* mammalian cell test systems. C1 – C4 hydrocarbons that have been tested include ethylene, butylene, and propylene. Please see Appendix 4 for experimental systems and references. A study on 2-butene was selected for the C1 – C4 hydrocarbon bacterial mutagenicity key study.

2-Butene (mixed isomers; 42.4% cis, 55.3% trans) was evaluated in an OECD Guideline #473 chromosome aberration assay in Sprague Dawley rat primary blood lymphocyte cultures. Metabolic activation system: Sprague Dawley male rat liver (S9 fraction) -20% S9 fraction in S9 mix, (10% v/v S-9 mix/flask) Aroclor 1254 induced; 500 mg/kg single ip injection 5 days before sacrifice. Atmospheres of varying concentrations of butene (0.0, 10, 20, 40, 50, 60, 80, 100%) were generated by mixing 2-butene with clean dry air, using precalibrated gas flow meters as gas flow indicators. Mixtures passed through culture flasks for sufficient time (time not specified) to allow equilibration of the system. Analytical determinations were performed by GC on syringe samples of test atmospheres at representative concentrations. Blood samples were drawn from male rats (Sprague Dawley -CD-1, ages 8-20 wks. from CharlesRiver UK); cells were grown in RPMI medium supplemented with 10% fetal calf serum, 25 mM Hepes and antibiotics, at 37 degrees C in a humidified atmosphere of 5% carbon dioxide in air. Duplicate cultures were incubated for 48 hrs, then transferred to tubes, centrifuged and culture medium drawn off and saved. Cells were resuspended in flasks, in fresh culture medium with or without S9 metabolic activation mix and exposed to appropriate concentrations of 2-butene or control materials. Flasks were sealed and shaken to maximize cell exposure for 4 hrs +S9 or 20 hrs -S9. Cells exposed to 2-butene + S9 were resuspended after 4 hrs in original culture medium; one group was harvested at 20 hrs (16 hr recovery), the other at 30 hrs (26 hr recovery) after initiation of treatment; -S9 cultures were harvested after 20 full hours exposure to butene-2. Positive controls were ethyl methyl sulfonate (500 μg/ml) –S9, cyclophosphamide (4.2 μg/ml) +S9; gaseous control was vinyl chloride (50%) in 20 hr group –S9 and 30 hr group +S9. Negative control was clean, dry air. Frequency of cells with aberrations (± gaps) and frequency of polyploid cells (duplicate culture data pooled) were compared with concurrent vehicle control using Fisher's Exact Test. The cytotoxic concentrations of 2-butene were 50% and 80% with and without metabolic activation, respectively. Control compounds performed appropriately. 2-Butene did not induce significant dose-related increases in frequency of structural chromosome aberrations or polyploid cells at any concentration level at any harvest period either in the presence or absence of a liver enzyme metabolizing system. 2-Butene was not clastogenic to rat lymphocytes *in vitro* (Wright, 1992).

Negative for *in vitro* non-bacterial genotoxicity

C5 – C6 Light End Naphtha Hydrocarbons
Unleaded gasoline was tested in the Ames Microbial mutation assay in *Salmonella typhimurium* and *Saccharomyces cerevisiae* with and without metabolic activation from an Aroclor-induced rat liver homogenate mixture. *Salmonella* strains TA100, TA1535, TA1537, TA1538, TA98 and yeast strain D4 were employed. Based on preliminary cytotoxicity assays, concentrations of gasoline in dimethylsulfoxide were administered to all 5 *Salmonella* tester strains at doses of 0.375, 0.75, 1.5 and 3.0% and to yeast at doses of 0.625, 1.25, 2.5, and 5.0%. For plate assays, test material was added to cells in broth. The contents of the test tubes of broth plus test material were poured over selective agar plates. Plates were incubated at 37^0C for 48 hours, then removed from the incubator and revertant cells were counted. In the suspension tests, bacteria and yeast cultures were grown in complete broth. The cells were removed, washed and exposed to the test material. For the yeast cells exposure to gasoline was for 4 hours and bacterial cell exposure was for 1 hour. Aliquots of the cells were plated onto the appropriate complete media. After suitable incubation periods, the number of revertant colonies was counted. In the plate test**,** there was no increase in revertant colonies caused by exposure to gasoline at any concentration. The results in this assay were negative both with and without metabolic activation. In the suspension test without activation, slight increases were observed at the high dose levels with TA100, TA1537 and TA1538. However the responses were not sufficiently high to meet the criteria for positive responses. The increases with TA98 could not be reproduced in a repeat trial. In the suspension test with activation, scattered increases were found at one or more dose levels but were not reproducible in a repeat trial. Therefore, gasoline was not a mutagen in this test system. (API, 1977)

Negative for *in vitro* bacterial mutagenicity

Gasoline diluted in acetone, has been tested in a mouse lymphoma (L5178Y TK+/-) forward mutation assay. For the mutation assay the lymphoma cells were exposed for 5 hours to test material at concentrations ranging from 0.065 to 1.04 µl/ml with and without metabolic activation from Aroclor-induced rat liver S-9 homogenate mixture. After exposure to the test material, the cells were allowed to recover for 3 days and then cultures were selected for cloning and mutant selection. Surviving cell populations were determined by plating diluted aliquots in non-selective growth medium. A mutation index was derived by dividing the number of clones formed in the BUdR-containing selection medium by the number found in the same medium without BUdR. The ratio was then compared to that obtained from other dose levels and negative control values. Positive control compounds were ethyl methane sulfonate (EMS) for non-activated cultures and dimethylnitrosamine (DMN) for metabolically activated cultures. Little toxicity was observed with the test material. All results for gasoline from the non-activation assay were negative. The results from the activation assay were also considered to be negative. There was an increase in the number of mutants at the 0.52 µl/ml concentration but this appeared to result from a slight increase in the number of viable clones. There was no trend indicating a dose-related response and therefore, the increases were not believed to be compound related. Gasoline was not mutagenic in this mammalian cell system. (API, 1977)

Negative for *in vitro* non-bacterial genotoxicity

In Vitro Genetic Toxicity Conclusion
The majority of the Refinery Gases Category components are negative for *in vitro* genotoxicity. The exceptions are: benzene and 1,3-butadiene, which are genotoxic in bacterial and mammalian *in vitro* test systems; ethanethiol which was positive in a CHO SCE study; and methanethiol and hydrogen sulfide, which were equivocal in a non-bacterial assay (read-across from methanethiol sodium salt). The only one of these genotoxic constituents that is found in refinery gas streams in any significant concentration is hydrogen sulfide (up to 45%). Benzene and butadiene are found at concentrations up to approximately 2%; ethanethiol and methanethiol are not found above approximately 0.5 or 1%, respectively. It is thought to be unlikely that the mutagenic potential of these four constituents would be expressed at such low concentrations in the refinery gas streams; mutagenic concentrations of these gases would be above the lower explosive limit.

7.4 In Vivo Genetic Toxicity

Ammonia
There are early (1934) *in vivo* genetic toxicity tests on ammonia, however the validity of the results have been called into question due to excessive (98%) toxicity at doses that suggested weak genotoxicity[6]. A more current study has been conducted on ammonium chloride, which was evaluated in a micronucleus assay in male mice. Mice were administered a single intraperitoneal injection (i.p.) injection of 0, 62.5, 125, 250, 500 mg/kg ammonium chloride. Separate groups of mice received four i.p. injections over 24 hours at dosed of 31.3, 62.5, 125, and 250 mg/kg. The maximum dose of ammonium chloride was determined by pilot experiments using the multi-sampling at multi-dose levels method to determine the MTD (maximally tolerated dose). Mice were killed 24hr after the single or first of four i.p injections and femoural marrow cells were flushed out with fetal bovine serum and fixed with methanol and stained with Giemsa. One thousand polychromatic erythrocytes per mouse were scored using a light microscope and the number of micronucleated polychromatic erythrocytes (MNPCE) was recorded. The number of MNPCE was comparable to control values for all treatment groups. Ammonium chloride was not genotoxic in this assay (Hayashi et al., 1988).

Negative for *in vivo* genotoxicity as assessed using ammonium chloride

Carbon monoxide
No *in vivo* genotoxicity available.

Hydrogen sulfide
There are no *in vivo* genotoxicity data available for hydrogen sulfide. Read across data from mercaptans (methanethiol) is appropriate for this endpoint. In an OECD 474 mouse micronucleus test, animals were exposed to 0, 114, 258 and 512 ppm methanethiol. There was no significant increase in micronucleus frequency at any exposure level (ELF ATOCHEM, 1997; MTC, 2001).

Negative for *in vivo* genotoxicity

Methanethiol
The genotoxic potential of nose-only inhalation exposure of methyl mercaptan to induce micronucleus formation in bone marrow erythrocytes was determined in Swiss-Webster mice. In the dose-range finding study, three mice per sex per treatment group received a single 6-hour nose-only inhalation exposure to methyl mercaptan at 112, 374, and 570 ppm. A control group, consisting of three male and three female mice, received air only. Mice were observed daily from the start of treatment until death or sacrifice. The concentration ranges for the low- and mid-concentrations exceeded the protocol criterion of 10%. These deviations are judged not to have had a significant adverse effect on the study. In the definitive experiment, 15 mice per sex per treatment group were exposed to methyl mercaptan by nose-only inhalation at 114, 258, or 512 ppm. Five mice per sex per group were sacrificed 24, 48, and 72 hours after exposure to assess cytotoxicity and micronucleus formation. An air-exposed control group of male and female mice and a urethane positive control group of male mice were treated similarly and evaluated concurrently with the methyl mercaptan-treated groups. In male mice, none of the individual dose groups had a statistically significant increase in MN frequency. Using the Cochran-Armitage test for a trend in binomial proportions, a statistically significant upward trend in micronucleus (MN) frequency was observed in female mice sacrificed at 24 hr after exposure to the methyl mercaptan. However, the MN frequency in the control group was lower than the laboratory historical value (0.21%) for females of this strain of mice, and none of the individual dose

[6] The 2004 ATSDR Ammonia Toxicological profile (http://www.atsdr.cdc.gov/toxprofiles/tp126.html) concludes that "Taken together [i.e. weight of evidence], the data indicate that ammonia and ammonium ion may have clastogenic and mutagenic properties." However, ATSDR and others (WHO, 1986; BIBRA, 1995; Clement Associates, Inc. 1990) have noted that *in vivo* activity in *Drosolphia melanogaster* (not reported in this paper) was only evident at doses that killed 98% of the flies, which casts significant doubt on the validity of results.

groups had a statistically significant increase in micronucleus frequency. Methanethiol was not an *in vivo* mutagen in this test system (ELF ATOCHEM, 1997; MTC, 2001).

Negative for *in vivo* genotoxicity

Ethanethiol
There are no *in vivo* genotoxicity data available for ethanethiol. Read across data from methanethiol is appropriate for this endpoint. In an OECD 474 mouse micronucleus test, animals were exposed to 0, 114, 258 and 512 ppm methanethiol. There was no significant increase in micronucleus frequency at any exposure level (ELF ATOCHEM, 1997; MTC, 2001).

Negative for *in vivo* genotoxicity

Benzene
Micronucleus assay and SCE
The induction of chromosomal effects under *in vivo* conditions after short term inhalation of benzene was evaluated in Sprague Dawley rats and DBA/2 mice in micronucleus and sister chromatid exchange (SCE) assays. Induction of SCEs is not a genotoxic event, per se, since no genetic material is lost and gene pairing of alleles remains intact. However, it does indicate an interaction with the DNA, which may or may not be confirmed as genotoxic in assays specifically designed to test for genotoxicity. Five male mice per treatment group were exposed to benzene vapors by inhalation at 0, 10, 100, or 1,000 ppm. Five male rats per treatment group were exposed to 0.1, 0.3, 1, 3, 10, or 30 ppm benzene for 6 hours. An air-exposed control group of 10-20 male mice/rats were treated similarly and evaluated concurrently with the benzene-treated groups. Exposure chamber atmospheres were analyzed hourly for the top two benzene concentrations and two to three times per hour for the other doses. The animals were killed 18 hours after exposure and peripheral blood lymphocytes and femoral bone marrow samples were taken and slides prepared. The lymphocytes were cultured in the presence of liposaccharides or concanavalin-A to stimulate blastogenesis for SCE analysis. 5-Bromo-2-deoxyuridine was added 24 hours after culture initiation and the cultures harvested at 60 hrs (mice) or 52 hrs (rats) following a 4 hr demecolcine treatment. Two or three slides were prepared per animal for SCE analysis. Slides from five treated and three to five concurrent control animals were coded, combined, and randomized prior to analysis. Both parametric (Student t test) and nonparametric (Mann-Whitney U test) statistics were used to analyze the data. Polychromatic erythrocytes (PCEs) in the prepared bone marrow samples (one to four stained slides per animal) were assayed for micronuclei.1000-2000 PCEs were analyzed from each animal. 1000 nuclei and 100 metaphases were scored consecutively for mitotic index and cell cycle kinetics, respectively. A one-tailed Student's t test was used to compare the micronuclei frequencies in the benzene exposed animals to controls. Short term exposures to low concentrations of benzene induced statistically significant increases in SCEs in lymphocytes and polychromatic erythrocytes (micronuclei) in rats and mice (Erexson, 1986).

Positive for induction of non-bacterial SCEs

1,3-Butadiene
The genotoxic potential of nose-only inhalation exposure of butadiene to induce micronucleus formation in peripheral and bone marrow erythrocytes was determined in rats and mice. 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 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. 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. This effect was statistically significant at 500 ppm with the Student's t test, 2-tailed. An apparent decrease of the polychromatic to normochromatic ratio in a dose-dependent way was observed, but was not statistically significant with the linear regression test. 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. 1,3-butadiene was active in inducing micronuclei in peripheral

blood and bone marrow erythrocytes in mice at levels >50 ppm, but not in rats. The genotoxic effects observed in this study parallel the species differences observed in cancer studies (Autio, 1994).

Positive for *in vivo* genotoxicity

C1 – C4 Hydrocarbons
Hydrocarbons in the C1 – C4 range were not mutagenic in several *in vivo* micronuclei studies at concentrations up to 22,000 ppm. The C1 – C4 hydrocarbons that have been tested include liquified petroleum gas (primarily butane and propane), ethylene, propylene, butylene, and isobutylene. Please see Appendix 4 for experimental systems and references. The following mouse micronucleus assay on 1-butene is representative of the negative in vivo mutagenicity studies for the C1 – C4 HCs.

The genotoxic potential of nose-only inhalation exposure of 1-butene to induce micronucleus formation in bone marrow erythrocytes was determined in Swiss-Webster mice. 1-Butene was premixed with ambient air and introduced into inhalation chambers containing groups of mice (10 M, 10 F) at concentrations of 0, 1000, 9000,or 22,000 ppm 2 hrs/day for 2 days. One half of each group was killed on day 3 and the remainder on day 4 following exposure. One group (15 M, 15 F) exposed for one day to 22,000 ppm was killed on days 2, 3, 4 after treatment (5/sex/day). Test concentrations were monitored each day by gas chromatography. Positive control mice given cyclophosphamide (75 mg/kg) ip daily for 2 days were killed on day 3. Slides of bone marrow smears were prepared, stained with May-Grunewald/Giemsa stain and examined microscopically. For each mouse, 1000 polychromatic erythrocytes and all mature erythrocytes (normochromatic erythrocytes) were counted. Data collected included group mean body weights for each day, total polychromatic erythrocytes total normochromatic erythrocytes, polychromatic erythrocytes with micronuclei, and normochromatic erythrocytes with micronuclei. Values from treated groups for daily mean body weights, group means and std. dev. for polychromatic erythrocytes with micronuclei, (and group mean ratios of polychromatic erythrocytes to normochromatic erythrocytes 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 polychromatic erythrocytes at any dose level with a dose related response evident. Results were considered equivocal if only one of these criteria was met. 1-Butene given by inhalation 2 hrs/day for 2 days to mice had no effect on the frequency of micronucleated erythrocytes in bone marrow. Under these test conditions, 1-butene did not induce chromosome damage (Khan and Ward, 1985).

Negative for *in vivo* genotoxicity

C5 – C6 Light End Naphtha Hydrocarbons
Baseline Gasoline vapor condensate [BGVC], a 20% light fraction of a whole unleaded gasoline was tested in the rat micronucleus assay according to USEPA OPPTS 870.5395 as a satellite study to the 13 week inhalation study described in Section 7.1.2 Repeated Dose Toxicity. Sprague Dawley rats (5/sex/group) were exposed by whole body inhalation to target concentrations of 0, 2000, 10000, 20000mg/m^3 (actual concentrations 0, 2050, 10,153 and 20,324 mg/m^3) BGVC for 4 weeks, 6hr/day, 5 days/week. A separate positive control group was treated with 40mg/kg cyclophosphamide by intraperitoneal injection 24 hours prior to sacrifice. Rats were killed 24 hours after the 20th exposure and bone marrow from both femurs of each rat was prepared as smears on microscope slides. Slides were stained by the modified Feulgen method. One smear from each rat was examined for the presence of micronuclei in 2000 immature erythrocytes and cytotoxicity was determined by the ratio of immature erythrocytes in at least 1000 erythrocytes. The incidence of micronucleated mature erythrocytes was also recorded. BGVC did not cause statistically significant increases in micronucleated immature erythrocytes or micronucleated mature erythrocytes at any dose level. There was no cytotoxicity or a decrease in the proportion of immature erythrocytes observed. Baseline Gasoline Vapor Condensate did not induce cytogenetic damage in this test system. NOAEL ≥ 20324mg/m^3. (API, 2005b)

BGVC was also tested with a separate satellite group for the induction of sister chromatid exchange [SCE- a non-SIDs endpoint], using an in vivo/in vitro protocol. Sprague Dawley rats (5/sex/group) were exposed by whole body inhalation to target concentrations of 0, 2000, 10000, 20000mg/m^3 (actual concentrations 0, 2050, 10,153 and 20,324 mg/m^3) BGVC for 4 weeks, 6hr/day, 5 days/week. A separate positive control group was treated with 5mg/kg cyclophosphamde by intraperitoneal injection 24 hours prior to sacrifice. Rats were killed 24 hours after the

20th exposure. Blood (2-4ml) was collected from the abdominal aorta, cultured within 24 hours and incubated at 37^0C for 21 hours. Cells were then exposed to 5µg/ml bromodeoxyuridine. After 68 hours from culture initiation, 0.2µg/ml colcimide was added to each culture flask to arrest cell division and incubation continued for 4 hours. At 72 hours total elapsed culture time, cells were collected, washed and fixed. Slides were prepared for microscopic evaluation. A minimum of 25 second-division metaphases per animal was scored for SCE. At least 100 consecutive metaphases per animal were scored for the number of cells in 1st, 2nd, and 3rd division metaphases as an indicator of toxicity (cell cycle delay) and 1000 cells were scored for mitotic index per rat. Statistically significantly increased SCE frequency was observed at all 3 dose levels in females and at the 10153 and 20324mg/m^3 levels for males. Increases in average generation time were also observed but no appreciable differences in mitotic indices were seen for any test group compared to controls. Although the SCE assay demonstrated interaction of BGVC and DNA, it was not considered definitive for clastogenic activity since no genetic material was unbalanced or lost, but rather a biomarker of exposure. Negative results in a parallel micronucleus assay, which visualizes actual cytogenetic damage demonstrate that BGVC is not a clastogenic material (API, 2005c).

Negative for *in vivo* genotoxicity

In Vivo Genetic Toxicity Conclusions

The majority of the Refinery Gases Category components are negative for in vi*vo* genotoxicity**.** The exceptions are benzene and 1,3-butadiene, which are genotoxic in *in* vi*vo* test systems**.** Benzene and 1,3-butadiene are found at no more than approximately 2% in refinery gas streams. It is thought to be unlikely that the mutagenic potential of benzene or butadiene would be expressed at such low concentrations in the refinery gas streams; mutagenic concentrations of these gases would be above the lower explosive limit.

7.5 Developmental Toxicity

Ammonia

From 2-4.5 months of age, gilts (a young sow that has not been pregnant or given birth) were exposed naturally to *Mycoplasma hyponeumoniae* and *Pasteurella multocida*, which cause enzootic pneumonia and atrophic rhinitis, respectively. The species tested were Yorkshire x Hampshire x Chester White pigs. At 4.5 months of age, the gilts were moved to one of two rooms and exposed to either low (mean 7 ppm) or moderate (mean 36 ppm) aerial concentrations of ammonia for continuous exposure for 6 or 10 weeks. There was no untreated control group. Each exposure group consisted of 40 individuals. In the room with low ammonia concentration, manure was flushed weekly to maintain a 0.3 m depth. In the room with moderate ammonia concentration, manure accumulated to 0.48 m depth. Moderate aerial ammonia concentration was obtained initially and maintained by adding anhydrous ammonia from a steel tank. Mean Daily Gain (MDG) was determined by weighing the gilts biweekly. Half the gilts from each exposure concentration were sacrificed after 6 weeks. The remaining gilts were maintained in their respective environments, exposed daily to mature boars, bred at first estrus, and sacrificed at day 30 of gestation. At the end of two weeks, gilts in the moderate exposure group weighed less than those in the low exposure. After 2 weeks gilts acclimated and the Mean Daily Gain (MDG) was similar for the rest of the experiment. The gilts sacrificed at 6 weeks showed that the animals in the low exposure were heavier. At day 30 of gestation, number of fetuses, fetal length, and were all similar between the two groups. These data indicate that, relative to the low, 7 ppm exposure group, exposure of gilts to mean aerial ammonia concentrations of 36 ppm depressed MDG for 2 weeks but failed to alter onset of puberty, litter size, fetal length, and fetus-to-corpus luteum ratio through day 30 of gestation. There was no developmental or reproductive toxicity to pigs in this assay; the NOAEL ≥ 35 ppm, the highest dose of ammonia tested (Diekman *et al*., 1993).

NOAEL (pigs) ≥ 35 ppm (highest dose tested)

Carbon monoxide

The potential developmental toxicity effects of carbon monoxide exposure were evaluated in CD-1 mice. Female albino CD-1 mice were bred overnight with males of the same strain, and the day a copulation plug was found was designated as gestation day 1. The pregnant animals were exposed continuously to 0, 65, 125, 250, or 500 ppm

carbon monoxide in air in Plexiglas environmental chambers from gestation day 7 to 18. The concentration of carbon monoxide was monitored at each chamber inlet by carbon monoxide detector. The animals were killed on gestation day 18, and their uterine horns were examined for gross malformations. One-third of the fetuses were examined for skeletal abnormalities. Litter means for fetal weight, number of live fetuses, and number of dead or resorbed fetuses was used to test for carbon monoxide effects on weight and fetal mortality. Analysis of variance and Student·Neuman-Keuls multiple range tests were used for the comparison between control and test groups for fetal weights and mean number of dead or resorbed fetuses per litter. Mean percent fetal mortality was obtained by calculating the mean of litter means. Results are based on data from 17 litters for each concentration of carbon monoxide. Further studies using the same experimental protocol, but at exposure levels of 0, 65, or 125 ppm carbon dioxide from day seven to 18 of pregnancy examined carbon monoxide effects on neonatal reflex development. No sign of maternal toxicity was observed under the conditions of exposure. However, effects were observed in the offspring. The mean percent fetal mortality per litter from mothers exposed to carbon monoxide at 0, 65, 125, 250, or 500 ppm was 4.52, 5.89, 12.50, 15.50, and 55.30, respectively. The mean number of dead or resorbed fetuses per litter in the high-dose group was significantly greater than the control value. Weights of fetuses from 125, 250, and 500 ppm carbon monoxide-exposed mothers were significantly decreased when compared to weights of controls. Fetal weight was not significantly influenced by 65 ppm carbon monoxide exposure, although the decreased value compared to controls was suggestive of an effect. A small number of skeletal anomalies (lack of ossification) were observed in fetuses from all groups, however, these anomalies were not dose dependent. Data suggest that maternal carbon monoxide exposure to as low as 125 ppm can affect fetal growth and higher exposure concentrations impair fetal viability. The fetus appears to be sensitive to chronic carbon monoxide exposure and this sensitivity is dose dependent. Results from the follow up study indicated that parental carbon monoxide exposure to levels as low as 65 ppm altered the righting reflex of neonates, indicating damage to the developing central nervous system. No signs of maternal toxicity were observed. Exposure did not affect the number of live pups born per litter or their birth weight. At 125 ppm, prenatal carbon monoxide exposure significantly increased the time required by neonates for righting reflex on day one of birth and negative geotaxis on day 10. Both doses (65 and 125 ppm) significantly decreased mean aerial righting score of pups on day 14. Findings suggest that at low concentrations, prenatal carbon monoxide exposure may lead to retarded reflex development in neonates in a dose dependent manner. Fetal acidosis, hypotension, and hypercarbia which accompany severe intrauterine hypoxia may contribute to the retarded reflex development of pups. The developmental LOAEL was ≤ 65 ppm (Singh and Scott, 1984; Singh, 1986).

LOAEL (CD-1 mice) ≤ 65 ppm (lowest dose tested)
Maternal NOAEL (CD-1 mice) ≥ 500 ppm (highest dose tested)

Hydrogen sulfide
An OECD guideline 421 reproductive and developmental toxicity study was conducted on hydrogen sulfide gas in Sprague Dawley rats as concentrations of 0, 10, 30, and 80 ppm. This study investigated the effects of perinatal exposure by inhalation to hydrogen sulfide on pregnancy outcomes, offspring prenatal and postnatal development, or offspring behavior. Virgin male and female Sprague-Dawley rats (12 rats/sex/concentration) were exposed (0, 10, 30, or 80 ppm hydrogen sulfide; 6h/day, 7 days/week) for 2 weeks prior to breeding. Exposures continued during a 2-week mating period (evidence of copulation = GD 0) and then from GD 0 through GD 19. Exposure of dams and their pups (eight rats/litter after culling) resumed between PND 5 and 18. Adult male rats were exposed for 70 consecutive days. Offspring were evaluated using motor activity (PND 13, 17, 21, and 60 ± 2), passive avoidance (PND 22 ± 1 and 62 ± 3), functional observation battery (PND 60 ± 2) acoustic startle response (PND 21 and 62 ± 3) and neuropathology (PND 23 ± 2 and 61 ± 2). There were no deaths and no adverse physical signs observed in F0 male or female rats during the study. A statistically significant decrease in feed consumption was observed in F0 male rats from the 80 ppm hydrogen sulfide exposure group during the first week of exposure. There were no statistically significant effects on the reproductive performance of the F0 rats as assessed by the number of females with live pups, litter size, average length of gestation, and the average number of implants per pregnant female. Exposure to hydrogen sulfide did not affect pup growth, development, or performance on any of the behavioral tests. The F0 male and female systemic toxicity NOAEL was 30 ppm and 80 ppm, respectively. The reproductive and developmental NOAELs for this study were ≥ 80 ppm, the highest dose tested (Dorman *et al*., 2000).

Developmental NOAEL (Sprague Dawley rats) ≥ 80 ppm (highest dose tested)
Parental Male systemic LOAEL (Sprague Dawley rats) = 80 ppm

Parental Male systemic NOAEL (Sprague Dawley rats) = 30 ppm
Parental Female systemic NOAEL (Sprague Dawley rats) ≥ 80 ppm (highest dose tested)

Methanethiol
There are no developmental toxicity studies on methanethiol. Read across data from hydrogen sulfide is appropriate for this chemical. The developmental toxicity of NOAEL ≥ 80 ppm from hydrogen sulfide will be read across to this chemical. (Dorman *et al*., 2000; also see Mercaptan Council HPV submission: http://iaspub.epa.gov/oppthpv/document_api.download?FILE=c13333tp.pdf).

NOAEL (Sprague-Dawley rats) ≥ 80 ppm (highest dose tested)

Ethanethiol
There are no developmental toxicity studies on ethanethiol. Read across data from hydrogen sulfide is appropriate for this chemical. The developmental toxicity of NOAEL ≥ 80 ppm from hydrogen sulfide will be read across to this chemical. (Dorman *et al*., 2000; MTC, 2001)

NOAEL (Sprague-Dawley rats) ≥ 80 ppm (highest dose tested)

Benzene
The developmental toxicity of benzene was evaluated in a series of three experiments. Female Swiss-Webster (Crl: CFW(SW)Br) mice (5-10 mice/concentration level) were exposed (0, 5, 10, or 20 ppm benzene, 6h/day, gestation days 6-15 in all experiments. In experiment 1, five benzene-exposed and five air-exposed pregnant mice were sacrificed on the 16th day of gestation, their uteri removed, and the number of live, dead, and resorbed fetuses recorded. Two male and two female fetuses were then randomly selected, weighed, and examined for any external gross morphological malformations. Peripheral blood samples were taken for red and white cell counts and for hemoglobin analysis. Livers were removed for enumeration of recognizable cells in the hematopoietic differentiating, proliferating pool (DPP). In experiment 2, five benzene-exposed and five air-exposed pregnant females were allowed to proceed through normal parturition. Two male and two female neonates were then randomly selected at 2 days of age and subjected to the same protocol as that described above with 16-day old fetuses. In experiment 3, five benzene-exposed and five air-exposed pregnant dams were allowed to proceed through normal parturition. At 6 weeks of age, one male and one female were randomly selected from each litter. Peripheral blood samples were obtained from tail veins for red and white cell counts and for hemoglobin analysis. These animals were then sacrificed and their spleen and femurs removed for enumeration of recognizable cells in the DPP. Peripheral and organ blood cell counts were determined, each benzene exposed animal having its own age-matched air control.

There was no evidence of maternal toxicity among dams exposed to any concentration of benzene tested as determined by maternal morbidity, mortality, or weight loss during the exposures. There was no evidence of non-hematopoietic toxicity among any of the fetal or neonatal progeny exposed *in utero* to any concentration of benzene studied. Litter sizes, male/female ratios, and body weights, as well as the numbers of dead, resorbed, or malformed fetuses, were all within control limits. In 2-day neonates, the 20 ppm exposure group showed significantly lower counts of late nucleated red cells and decreased counts of early nucleated red cells, whereas the numbers of blasts, dividing/nondividing granulocytes and lymphocytes were elevated. In 6-week old offspring, the 20 ppm exposure group showed a slightly higher numbers of blasts, dividing/nondividing granulocytes and lymphocytes in comparison to their age-matched controls. *In utero* exposures to 20 ppm benzene induced persistent, enhanced production of granulopoietic elements in the hematopoietic systems of offspring. The maternal NOAEL was ≥ 20 ppm. The developmental LOAEL = 20 ppm, and the NOAEL = 10 ppm (Keller and Snyder, 1988).

LOAEL (mice) = 20 ppm
NOAEL (mice) = 10 ppm
Maternal systemic NOAEL ≥ 20 ppm

1,3-Butadiene
The developmental effects of 1,3-butadiene were evaluated in an OECD Guideline 414 teratogenicity study. Female Sprague Dawley 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, and 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. Analysis of variance for body weights, number of resorptions, implants, live, dead or affected fetuses per litter was performed. Significant differences among the groups were also analyzed by Duncan's multiple range tests or arcsine transformation of the response proportion. Binary-response variables between groups were compared using chi-square or Fisher's exact test. 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. There was no evidence of teratogenicity or adverse reproductive effects in any of the exposed groups. Based on decreased body weight gains, the maternal systemic toxicity LOAEL and NOAEL were 1000 ppm and 200 ppm, respectively. The NOAEL for developmental effects was ≥ 1000 ppm (Morrissey *et al.*, 1990).

Developmental (Sprague Dawley rats) ≥ 1000 ppm (highest dose tested)
Maternal systemic LOAEL = 1000 ppm
Maternal systemic NOAEL = 200 ppm

C1 – C4 Hydrocarbons
The developmental toxicity of a racemic mixture of 2-butene (cis and trans, 95% purity) was assessed an OECD 422 Combined Repeated Dose Toxicity with the Reproductive/Developmental Toxicity Screening Test. Twelve male and 12 female Wistar rats per group were exposed to 0, 2500 or 5000 ppm 2-butene for 6 hours/day, 7 days/week. Males were exposed for 39 to 46 days; females were exposed two weeks prior to mating, through mating, and to gestation day 19. Body weights and food consumption were recorded. At study termination, hematology and clinical chemistries were conducted on blood, gross necropsies were conducted, organs weights were recorded and tissues processed for microscopic evaluation. Control and high dose groups, only, were evaluated microscopically. Body weight change was lower for male rats in the first and fourth weeks of exposure in the 2500 ppm group and in the first week in the 5000 ppm group. Female body weights were reduced in the 2500 ppm group at 14 days of exposure and the 5000 ppm group at 7 and 14 days of exposure. Female body weights were comparable during mating and gestation, but were reduced in the 5000 ppm group on lactation day 1. Male rats in both exposure groups had increased total white cell and lymphocyte counts, however there was no dose-response and counts were within historical control range. A decrease in plasma calcium concentration was observed in high dose males. No developmental (or reproductive) toxicity was observed. No treatment-related increase in pre-implantation loss occurred. Post-implantation loss was slightly increased in the 5000 ppm exposure group, however it was within the historical control range. The total number of live births in the exposed groups was higher than controls. In the control and 2500 ppm groups, one pup died between days 1 and 4 of lactation; the viability index was 97 to 100%. Mean body weights of pups was slightly but not significantly lower in the treated groups, which may be explained by the higher number of pups in the two treatment groups compared to controls. No structural changes were noted in treated pups either during lactation or at necropsy. The systemic toxicity NOAEL was 2500 ppm. The developmental toxicity NOAEL was $\underline{\geq}$ 5000 ppm (Waalkens-Grendsen and Arts, 1992). In selecting 2-butene to represent the developmental toxicity of the C1 – C4 HC fraction, the entire C1-C4 HC fraction concentration is assumed to be 100% 2-butene for purposes of calculating C1 – C4 HC developmental toxicity ranges for each refinery gas.

Developmental Toxicity (Wistar rats) NOAEL $\underline{\geq}$ 5000 ppm (highest dose tested)
Parental Systemic Toxicity (Wistar rats) LOAEL = 5000 ppm
Parental Systemic Toxicity (Wistar rats) NOAEL = 2500 ppm

C5 – C6 Light End Naphtha Hydrocarbons
A developmental toxicity study in rats of Baseline Gasoline Vapor Condensate (BGVC), a 20% light fraction of whole unleaded gasoline was performed according to OPPTS 870.3600, 870.3700 and OECD 414 guidelines. This test material was a representative evaporative emission tested under the USEPA 211(b) Fuels and Fuel Additives Health Effects Testing Program (1994b). BGVC was administered to 25 confirmed-mated female Crl:CD-1®(ICR)BR

mice/exposure group at target concentrations of 0, 2000, 10,000, and 20,000 mg/m^3 (mean analytical concentrations 0, 2086, 10625 and 20,903 mg/m^3; 0, 680, 3463, and 6814 ppm) in air. The animals were exposed daily for six hours from Gestation Day 5 through Gestation Day 17. On GD 18, animals were sacrificed and cesarean sections (C-sections) were performed. Gross necropsies were performed, uterine weights with ovaries attached were recorded, uterine contents were examined, and the required uterine implantation data were recorded. All fetuses were weighed, sexed externally, and examined externally for gross malformations. There were no statistically significant differences from control in the treated groups in the incidence of fetal observation. Slight emaciation was the only clinical sign noted during the study and was noted in one of the dams in the highest exposure group (6814 ppm) on Gestation Day 11. Maternal toxicity was evident as statistically significant differences in mean gestation body weight and mean gestation body weight change in the 6,814 ppm target group. Statistically significant reduced fetal body weights, compared with the control fetal weights, were noted in the 3,463 and 6,814 ppm target concentration groups. The reduction of these fetal weights occurred in the absence of statistically significant reductions in maternal body weight and body weight change in the 3,463 mg/m^3 target concentration group. Therefore, the mouse NOAEL for this study was established at the 680 ppm and the mouse LOAEL was 3,463 ppm (API, 2009). A developmental toxicity study was also conducted in Sprague-Dawley rats using the same test material and protocol. There was no maternal or developmental toxicity in the rats. The rat maternal and developmental toxicity NOAEL was ≥ 6729 ppm, the highest dose tested (API, 2008b).

LOAEL (CD-1 mice) = 3,463 ppm (10,635 mg/m^3)
NOAEL (CD-1 mice) = 680 ppm (2,086 mg/m^3)

Developmental Toxicity Conclusion

Developmental effects were induced by three of the 12 refinery gas constituents, benzene, carbon monoxide, and the C5 - C6 hydrocarbon fraction. No developmental toxicity was observed at the highest exposure levels tested for the other refinery gas constituents tested for this effect. The asphyxiant gases have not been tested for developmental toxicity. Based on LOAEL and NOAEL values, the order of acute toxicity of these constituents from most to least toxic is[7]:

Benzene (LOAEL = 20 ppm) > ammonia (NOAEL ≥ 35 ppm) > hydrogen sulfide (NOAEL ≥ 80 ppm) = methyl mercaptan (NOAEL ≥ 80 ppm) = ethyl mercaptan (NOAEL ≥ 80 ppm) > carbon monoxide (LOAEL ≤ 65 ppm) > butadiene (NOAEL ≥ 1,000 ppm) > C5 – C6 HCs (LOAEL = 3,463 ppm) > C1 – C4 HCs (NOAEL ≥ 5,000 ppm; assumed to be 100% 2-butene) > asphyxiant gases (hydrogen, carbon dioxide, nitrogen)

7.5 Reproductive Toxicity

Ammonia
From 2-4.5 months of age, gilts (a young sow that has not been pregnant or given birth) were exposed naturally to *Mycoplasma hyponeumoniae* and *Pasteurella multocida*, which cause enzootic pneumonia and atrophic rhinitis, respectively. The species tested were Yorkshire x Hampshire x Chester White pigs. At 4.5 months of age, the gilts were moved to one of two rooms and exposed to either low (mean 7 ppm) or moderate (mean 36 ppm) aerial concentrations of ammonia for continuous exposure for 6 or 10 weeks. There was no untreated control group. Each exposure group consisted of 40 individuals. In the room with low ammonia concentration, manure was flushed weekly to maintain a 0.3 m depth. In the room with moderate ammonia concentration, manure accumulated to 0.48 m depth. Moderate aerial ammonia concentration was obtained initially and maintained by adding anhydrous ammonia from a steel tank. Mean Daily Gain (MDG) was determined by weighing the gilts biweekly. Half the gilts from each exposure concentration were sacrificed after 6 weeks. The remaining gilts were maintained in their respective environments, exposed daily to mature boars, bred at first estrus, and sacrificed at day 30 of gestation. At the end of two weeks, gilts in the moderate exposure group weighed less than those in the low exposure. After 2 weeks gilts acclimated and the Mean Daily Gain (MDG) was similar for the rest of the experiment. The gilts sacrificed at 6 weeks showed that the animals in the low exposure were heavier. At day 30 of gestation, number of

[7] ranking is not precise since several values were the highest dose tested

fetuses, fetal length, and were all similar between the two groups. These data indicate that, relative to the low, 7 ppm exposure group, exposure of gilts to mean aerial ammonia concentrations of 36 ppm depressed MDG for 2 weeks failed to alter onset of puberty, litter size, fetal length, and fetus-to-corpus luteum ratio through day 30 of gestation. There was no developmental or reproductive toxicity to pigs in this assay; the NOAEL ≥ 35 ppm, the highest dose of ammonia tested (Diekman *et al*., 1993).

NOAEL (pigs) ≥ 35 ppm (highest dose tested)

Carbon monoxide
The reproductive toxicity of carbon monoxide was evaluated in Long Evans rats. Twelve to 16 sperm-positive female rats per group were exposed to 0, 30 or 90 ppm carbon monoxide on gestation days 3 to 20. The percentage of successful pregnancies was 100% in the control group. In rats treated with 30 ppm or 90 ppm carbon monoxide, the success rate was reduced in a dose-dependent manner; 69% and 38% success rates, respectively. The authors speculated that failure of blastocyst implantation accounted for the majority of the unsuccessful pregnancies in treated dams. Based upon post-implantation loss, the reproductive LOAEL was ≤ 30 ppm, the lowest dose tested (Garvey and Longo, 1979).

LOAEL (rat) ≤ 30 ppm (lowest dose tested)

Hydrogen sulfide
An OECD guideline 421 reproductive and developmental toxicity study was conducted on hydrogen sulfide gas in Sprague Dawley rats as concentrations of 0, 10, 30, and 80 ppm. This study investigated the effects of perinatal exposure by inhalation to hydrogen sulfide on pregnancy outcomes, offspring prenatal and postnatal development, or offspring behavior. Virgin male and female Sprague-Dawley rats (12 rats/sex/concentration) were exposed (0, 10, 30, or 80 ppm hydrogen sulfide; 6h/day, 7 days/week) for 2 weeks prior to breeding. Exposures continued during a 2-week mating period (evidence of copulation = GD 0) and then from GD 0 through GD 19. Exposure of dams and their pups (eight rats/litter after culling) resumed between PND 5 and 18. Adult male rats were exposed for 70 consecutive days. Offspring were evaluated using motor activity (PND 13, 17, 21, and 60 +/- 2), passive avoidance (PND 22 ± 1 and 62 ± 3), functional observation battery (PND 60 ± 2) acoustic startle response (PND 21 and 62 ± 3) and neuropathology (PND 23 ± 2 and 61 ± 2). There were no deaths and no adverse physical signs observed in F0 male or female rats during the study. A statistically significant decrease in feed consumption was observed in F0 male rats from the 80 ppm hydrogen sulfide exposure group during the first week of exposure. There were no statistically significant effects on the reproductive performance of the F0 rats as assessed by the number of females with live pups, litter size, average length of gestation, and the average number of implants per pregnant female. Exposure to hydrogen sulfide did not affect pup growth, development, or performance on any of the behavioral tests. The F0 male and female systemic toxicity NOAEL was 30 ppm and 80 ppm, respectively. The reproductive and developmental NOAEL for this study was ≥ 80 ppm, the highest dose tested (Dorman *et al*., 2000).

Reproductive NOAEL (Sprague Dawley rats) ≥ 80 ppm (highest dose tested)
Parental Male systemic LOAEL (Sprague Dawley rats) = 80 ppm
Parental Male systemic NOAEL (Sprague Dawley rats) = 30 ppm
Parental Female systemic NOAEL (Sprague Dawley rats) ≥ 80 ppm (highest dose tested)

Methanethiol
There are no reproductive toxicity studies on methanethiol. Read across data from hydrogen sulfide is appropriate for this chemical. The reproductive toxicity of NOAEL ≥ 80 ppm from hydrogen sulfide will be read across to this chemical. (Dorman *et al*., 2000; MTC, 2001).

NOAEL (Sprague-Dawley rats) ≥ 80 ppm (highest dose tested)

Ethanethiol
There are no reproductive toxicity studies on ethanethiol. Read across data from hydrogen sulfide is appropriate for this chemical. The reproductive toxicity of NOAEL ≥ 80 ppm from hydrogen sulfide will be read across to this chemical. (Dorman *et al*., 2000; also see Mercaptan Council HPV submission: MTC, 2001).

NOAEL (Sprague-Dawley rats) ≥ 80 ppm (highest dose tested)

Benzene
Male and female fertility have been investigated in laboratory animals in studies of different quality and validity via the inhalation route of exposure. There is one inhalation fertility study on female rats available (Kuna et al., 1992), in which female Sprague-Dawley rats were exposed to dose levels of 1, 10, 30, and 300 ppm benzene (6 h/day, 5 d/week) during premating and mating (10 weeks), gestation and lactation periods up to post-natal day 21. No effects on fertility were observed, however, this study was not considered adequate for estimations to the overall potential of benzene for fertility impairment with respect to both sexes. In addition, systemically toxic concentration levels were not tested. Consequently, it is more appropriate to use a well-conducted 90-day subchronic study to evaluate the potential reproductive hazards of benzene. The reproductive toxicity of benzene was assessed by evaluation of male and female reproductive organs in a 90-day subchronic study. This study investigated the systemic effects of a 13 week benzene (whole chamber, vapor) exposure by inhalation. Male and female CD-1 mice (40 mice/sex/dose) were exposed (0, 1, 10, 30, or 300 ppm benzene; 6h/day, 5 days/week) for 13 weeks. Criteria used to evaluate exposure related effects included behavior, body weights, organ weights, clinical pathology, gross pathology, and histopathology. All animals were observed twice daily, before and after exposure and on nonexposure days, for mortality and moribundity throughout the study. At weekly intervals animals were observed for signs of toxicity, weighed and individual body weights recorded. On study days 7, 14, 28, 56, and 91, blood samples were taken from randomly selected mice (20 mice/sex/group) for full range hematological and clinical chemistry examinations. Blood was collected for clinical pathology analyses from an additional 30 mice one day prior to the start of the study. For interim sacrifice on days 7, 14, 28, 56, and for terminal sacrifice on day 91, 20 mice/sex/group were randomly selected and killed. Complete necropsies were performed on all these animals and on animals found dead or sacrificed in a moribund condition during the study. With respect to reproductive organs, absolute testes weight and testes/terminal body weight ratios were determined for each animal that was necropsied at each interval. In addition, the following tissues from each animal necropsied at each sacrifice interval was taken and fixed: testes or ovaries, prostate or uterus, and mammary gland. Sections from the control and high-level groups at each sacrifice period were subject to histopathological examinations. The testes and ovaries of all animals at all exposure levels at the 91-day terminal sacrifice were examined microscopically. With respect to reproductive organs a statistically significant and exposure-time related decrease in absolute mean testes weights at sacrifices on days 28, 56, and 91, as well as in relative mean testes at sacrifices on days 59 and 91 occurred at the 300 ppm level (data not provided). Histomorphologic changes in reproductive organs were also reported at 300 ppm in male mice at the 91 day-interval (seven mice with minimal to moderately severe bilateral atrophy/degeneration of testes, 6 mice with moderate to moderately severe decrease in spermatozoa, 9 mice with minimal to moderate increase in abnormal sperm forms) but not in those sacrificed at the earlier intervals. At the 300 ppm dose level, four female mice showed bilateral ovarian cysts. The severity of gonadal lesions was greater in the males. Similar lesions were reported to be observed in both sexes also at lower dose levels, which the authors considered of doubtful biological significance, and it is assumed that these levels did not represent any significant changes from the controls. Other histopathological changes observed at the high-dose level included the thymus, femoral marrow, spleen, mesenteric lymph nodes, mandibular lymph nodes and the liver, the severity increasing with time. Based on bilaterial cysts in ovaries, atrophy/degeneration of testes, decrease in spermatozoa, and increase in abnormal sperm, the reproductive LOAEL and NOAEL for both sexes was 300 ppm and 30 ppm, respectively (Ward *et al.*, 1985).

LOAEL (male and female CD-1mice) = 300 ppm
NOAEL (male and female CD-1 mice) = 30 ppm

1,3-Butadiene
The reproductive toxicity of 1,3-butadiene was evaluated in an OECD Guideline #421 study in Sprague Dawley rats. Three groups of 12 male and 12 female SpragueDawley rats were exposed to 0, 300, 1,500, and 6,000 ppm 1,3-butadiene via whole-body inhalation exposure 6 h/day for 14 days prior to the breeding period and continuing throughout the gestation and lactation periods. A control group was exposed to clean, filtered air on a comparable regimen. For F0 dams, the daily inhalation exposures were suspended on gestation day 21 through lactation day 4, to avoid any confounding effects of exposure on nesting or nursing behavior. Exposures were resumed for these dams on lactation day 5. The F1 generation pups were exposed to 1,3-butadiene *in utero* and through nursing during

lactation until weaning. Beginning on postnatal day 21, one male and one female from each litter were exposed for seven consecutive days to the same concentration of 1,3-butadiene concentration as its dam. Beginning on postnatal day 28, one previously unexposed male and one previously unexposed female per litter were exposed for seven consecutive days to the same 1,3-butadiene concentration as its dam. Assessments of gonadal function, mating behavior, conception, gestation, parturition, lactation of the F0 generation, and the development of F1 offspring from conception through weaning and post-weaning exposure were included in this study. No adverse treatment-related effects on any parameter measured in either the F0 or F1 animals at the exposure level of 300 ppm. At 1,500 and 6,000 ppm , effects consisted of persistent reductions in body weight parameters in F0 and F1 males and females and transient reductions in food consumption (week 0-1) for F0 males and females. Adverse effects noted only at the high dose of 6,000 ppm consisted of clinical observations indicative of chromodacryorrhea, chromorhinorrhea, and salivation in F0 males and females as well as infrequent occurrences of dried red material in the perioral and perinasal regions of four exposed F1 pups (three males and one female). Based on the results of this study, an exposure level of 300 ppm was considered to be the NOAEL in rats for F0 parental systemic toxicity and for systemic toxicity for F1 animals following post-weaning 6-h daily exposures (postnatal day 21-27 or postnatal day 28-34). Parental systemic toxicity LOAEL and NOAEL was 1500 ppm and 300 ppm, respectively. The NOAEL for effects on gonadal function, mating behavior, conception, gestation, parturition, lactation of the F0 generation, and the development of F1 offspring from conception through weaning was considered to be ≥ 6,000 ppm (WIL Research Laboratories, 2003).

Reproductive NOAEL ≥ 6,000 ppm (highest dose tested)
Parental systemic LOAEL = 1500 ppm
Parental systemic NOAEL = 300 ppm

C1 – C4 Hydrocarbons
The reproductive toxicity of isobutane was assessed in an OECD 422 Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test. Neurotoxicity was also evaluated. The test substance was administered as a gas to Sprague Dawley CD rats (12/sex/main study group and 12 females/satellite group) at target concentrations of 900, 3000 and 9000 ppm (note: highest dose is 50% of the lower explosive limit) for 6 hours/day, 7 days/week for 2 weeks prior to mating initiation. Main study male rats were exposed during the mating and post-mating periods until euthanized for a minimum exposure of 28 days. Main study female rats (12/group) were exposed once daily (6 hours/day), 7 days/week for 4 weeks (minimum of 28 days). Satellite female rats were exposed once daily (6 hours/day), 7 days/week for at least two weeks prior to mating initiation. Satellite female rats continued to be treated once daily (6 hours/day) during mating. Once mated, satellite female rats were treated once daily (6 hours/day) during gestation days 0-19. Main study females were evaluated for subchronic effects and satellite females for reproductive effects only. The following parameters were evaluated in all animals: viability, clinical observations, body weights, feed consumption, functional observational battery (FOB), motor activity, clinical pathology (termination), organ weights, and macroscopic observations. Microscopic pathology was conducted in the main study control and high-exposure groups only). No parental systemic toxicity was observed. In the 9000 ppm group, 25% of the mated females did not become pregnant. Although not statistically significant, the reduction in the male and female fertility indices (75%) was considered exposure-related since it was below the concurrent control (100%) and the testing facility historical control values (mean 96.4%; range 87.5% - 100%). Mating index for the male rats treated with the test substance was comparable to the air control group. A statistically significant ($p < 0.05$) exposure-related increase in post-implantation loss was also observed for the 9000 ppm group of exposed female rats; mean losses of 0.8 ± 0.9 and 1.8 ± 0.8 for control and high exposure groups, respectively. These findings should be interpreted with caution due to the low statistical power associated with this screening level study due to the small number of animals per group (n=12). Consequently the data were interpreted as conservatively as possible; the two reproductive toxicity findings were attributed to isobutane exposure. All other reproductive endpoints were comparable to controls (number of pairs cohabited, number of pairs mated, mating index, gestation index, mean time to mating, mean gestation length, number of females completing delivery with stillborn pups/all stillborn pups, mean pre-implantation loss, mean pups delivered, live birth index, viability index). Pup endpoints (viabilty to day 4, weight and weight gain, sex ratio) were also comparable to air control pups. In conclusion, exposure of male and female rats to target concentrations of 900, 3000 or 9000 ppm of isobutane by whole-body inhalation for 4-6 weeks resulted in no general systemic/neurotoxic effects. A no-observed-adverse effect level (NOAEL) of ≥ 9000 ppm was determined for all general systemic/neurotoxic endpoints in this study. The NOAEL

for pup endpoints was 9000 ppm based on no effects in offspring survival, body weight and development up to post-natal day 4 (HLS, 2008). Based on decreased male and female fertility and increased post-implantation loss in the 9000 ppm group, the reproductive toxicity NOAEL was determined to be 3000 ppm. In selecting isobutane to represent the reproductive toxicity of the C1 – C4 HC fraction, the entire C1-C4 HC fraction concentration is assumed to be 100% isobutane for purposes of calculating C1 – C4 HC reproductive toxicity ranges for each refinery gas. This is a worst case approach as other alkane gases did not product reproductive effects when tested in studies of similar design (see Appendix 4).

Reproductive LOAEL (Sprague Dawley rats) = 9000 ppm
Reproductive NOAEL (Sprague Dawley rats) = 3000 ppm
Developmental NOAEL (Sprague Dawley rats) = 9000 ppm (highest dose tested)
Parental Systemic NOAEL (Sprague Dawley rats) = 9000 ppm (highest dose tested)

C5 – C6 Light End Naphtha Hydrocarbons
Reproductive toxicity was evaluated in a 2-generation inhalation study with Baseline Gasoline Vapor Condensate (BGVC), a 20% light fraction of whole unleaded gasoline according to OPPTS 870.3800. This test material was a representative evaporative emission tested under the USEPA 211(b) Fuels and Fuel Additives Health Effects Testing Program (1994b). BVCG was administered to Sprague Dawley rats (26/sex/group) at target concentrations of 0, 2000, 10000, and 20000mg/m^3 (actual concentrations 0, 2014, 10,319 and 20,004 mg/m^3) 6hr/day, 7 days/week for 10 weeks before mating and 2 weeks of mating. Exposure of parental females [P0] with confirmed matings was continued until Gestation Day [GD] 19 and suspended until postpartum day 5 to avoid inducing undue stress to the dams during birth and early lactation. P0 dams continued to be exposed to BGVC until sacrifice at weaning. At weaning of the F1 generation on postpartum day 28, one pup/sex/litter was chosen randomly to continue exposure as the F1 parental generation; littermates were never paired together. Exposure of the F1 parental generation to BGVC began at weaning with 10 weeks of pre-mating exposure and continued on the same schedule as the P0 parental generation through mating gestation and lactation. Physical observations, body weights and food consumption were monitored at least weekly during the study. After approximately 16 weeks of exposure, all parental males [P0 and F1] were sacrificed and all parental females [P0 and F1] were sacrificed on postpartum days 28. Females that failed to mate were sacrificed 25 days after the end of the mating period. Fourteen organs were weighed from all rats and tissues from these organs were examined microscopically from 10 rats from the control and 20000mg/m3 groups. Reproductive organs from all males and bred females in the control and high dose groups were examined. Sperm evaluations included motility, counts of testicular homogenization-resistant sperm and cauda epididymal sperm, and sperm morphology in the cauda epididymis. Ovary histopathology included evaluation of primordial follicle population, number of growing follicles and corpora lutea. Pups (F1 and F2 generations) were observed as soon as possible after delivery for sex, number of live and dead pups and pup abnormalities. Pups dead at delivery were identified as stillborn or liveborn/found dead based on lung floatation evaluation. Thereafter litters were observed twice daily. On LD 4, F1 litters with more than 10 pups were randomly culled to 10 pups with sex distribution equalized if possible. Pups were examined and weighed on LD1 (delivery day), 4 (pre-culled), 7, 14, 21 and 28. At weaning one pup/sex/group was selected for mating to produce the F2 generation. F1 pups [5/sex/group/assessment] not selected for F1 mating were evaluated for standard Tier 2 neuropathology [40 CFR79.66] or for glial fibrillary acidic protein (GFAP) assessments [40 CFR79.67] on postpartum day 28 [Results of the GFAP study are reported in a separate Neurotoxicity robust summary but the GFAP assay is considered beyond the scope of this document]. The remaining pups were sacrificed. Three pups/sex/litter in each group were selected for macroscopic examination and selected organs [brain, spleen, thymus] were weighed from one pup/sex/litter.

Exposure of rats to 2014, 10,319 and 20,004 mg/m^3 of BGVC resulted in decreased body weight gains in the P0 females and F1 males prior to mating in the 20004 mg/m³ exposed group. Increases in kidney weights in parental male animals exposed to the two higher exposure levels of vapor were consistent with alpha 2-microglobulin mediated nephropathy seen in male rats, a finding has been generally accepted not to be relevant to human risk assessment (USEPA, 1991). There was no effect at any of the exposure levels on reproductive performance in the study, including mating, fertility, parturition, lactation, offspring survival and development or maturation, in either the P0 or F1 generations. Pregnancy rates for control, 2014, 10,319 and 20,004 mg/m^3 groups were 96.0%, 96.2%, 92.3% and 100% respectively for P0 animals and 100%, 100%, 91.7% and 100%, respectively for F1 animals. There was no evidence of any neuropathology in F1 pups as a result of the exposures. The NOAEL for systemic toxicity [excluding kidney effects in male rats] is 10319mg/m³. The NOAEL for neurotoxicity in F1 animals is

>20,004mg/m³. The Reproductive NOAEL was ≥ 20,004mg/m³. These results are comparable to those seen in other gasoline studies (Mckee *et al*, 2000) and with the refinery streams representative of the 4 chemical classes (API, 2008c).

NOAEL (Sprague Dawley rats) ≥ 6521 ppm; (20,004 mg/m^3; highest dose tested)

Reproductive Toxicity Conclusions

Reproductive effects were induced by only two refinery gas constituents, benzene and isobutane (a constituent of the the C1-C4 hydrocarbon fraction). No reproductive toxicity was observed at the highest exposure levels tested for the other refinery gas constituents tested for this effect. The asphyxiant gases have not been tested for reproductive toxicity. Based on LOAEL and NOAEL values, the order of reproductive toxicity of these constituents from most to least toxic is[8]:

Carbon monoxide (LOAEL ≤ 30 ppm)> ammonia (NOAEL ≥ 35 ppm) > hydrogen sulfide (NOAEL ≥ 80 ppm) = methyl mercaptan (NOAEL ≥ 80 ppm) = ethyl mercaptan (NOAEL ≥ 80 ppm) > Benzene (LOAEL = 300 ppm) > butadiene (NOAEL ≥ 6,000 ppm) > C5 – C6 HCs (NOAEL ≥ 6,521 ppm) > C1 – C4 HCs (LOAEL = 9,000 ppm; assumed to be 100% isobutane) > asphyxiant gases (hydrogen, carbon dioxide, nitrogen)

7.6 Refinery Gases Human Health Effects Read Across Method

The mammalian health hazards associated with Refinery Gases were characterized by 12 gas constituents that occur in concentrations ranging from 0 – 99.9% in Refinery Gases. The 12 constituents used to characterize health-related SIDS endpoints for each of the 62 Refinery Gases in the category are:

- Inorganic Gases
  - Ammonia
  - Carbon Monoxide
  - Ethyl mercaptan
  - Hydrogen sulfide
  - Methyl mercaptan
- Hydrocarbon Gases
  - Benzene
  - 1,3-Butadiene
  - C1 – C4 Hydrocarbons
  - C5 – C6 Hydrocarbons
- Asphyyxiant Gases
  - Carbon dioxide
  - Hydrogen gas
  - Nitrogen gas

The endpoint toxicity values (acute LC50, reproductive toxicity LOAEL/NOAEL, etc.) for each gas constituent have been adjusted to account for dilution of the constituent in each refinery gas. This adjustment represents the calculated concentration of the refinery gas required to reach the toxicity value (LC50, LOAEL, etc.) corresponding to the gas constituent in its pure state. For example, if the LC50 for neat (100%) hydrogen sulfide is 444 ppm, the LC_{50} for a refinery gas containing only 20% (wt./v) hydrogen sulfide would be 2,220 ppm; *i.e.* it would take five times more of the refinery gas containing 20% hydrogen sulfide to reach the LC50 for hydrogen sulfide, when the refinery gas is diluted with air.

[8] ranking is not precise since several values were the highest dose tested

LOAEL values were used to characterize constituent hazards for repeated-dose, developmental, and reproductive toxicities; the NOAEL value was used only if a LOAEL has not been established for any constituent in the refinery gas. Similarly, for acute toxicity, measured LC50 values from experiments where mortality was observed and an LC50 value was experimentally derived, were used to characterize acute hazard for each refinery gas. Values for constituents where no mortality was observed at the highest exposure level tested (*i.e.* C1 – C4 and C5 – C6 HCs) were used only for streams that do not contain constituents with measured LC50 values.

There are more than one constituent in each refinery gas. Consequently, the constituent that is most toxic for a particular endpoint was used to characterize the hazard for the entire refinery stream for that endpoint. For all constituents except the C1 – C4 HC fraction, there is one toxicity value per endpoint per constituent; *i.e* constituents were either individual chemicals (*e.g.* hydrogen sulfide) or a complex refinery stream substance (C5 – C6 HC fraction). For the C1 – C4 HC fraction, the most toxic individual C1 – C4 HC (*e.g*. 2-butene) was selected to characterize the fraction. It is assumed that the C1 – C4 fraction is essentially 100% of the individual HC selected to represent the C1 – C4 fraction hazard value for each SIDS mammalian toxicity endpoint. The formula used to correct for gas constituent dilution, as well as a detailed example for using the calculation to develop the minimum – maximum concentration value range to characterize the potential hazard for a specific endpoint to a refinery gas follows.

Dilution correction calculation formula:

Toxicity value correction for dilution of a constituent in a specific refinery gas is calculated by:

$$CV_n = TV_{neat} / TC_n$$

CV_n = corrected endpoint toxicity value for refinery gas *n*
TV_{neat} = endpoint toxicity value for the neat (100%) constituent
TC_n = concentration of the constituent in refinery gas_n expressed as the decimal value for percent concentration (wt/v).

Dilution correction calculation example:

CASRN 68477-65-6 *Gases (petroleum), amine system feed* contains the following components presented as wt/v%:

- Hydrogen = 30 - 50%
- Ammonia = 0.1 – 10%
- Hydrogen sulfide = 10 – 25%
- Carbon monoxide = 0.5 – 15%
- Carbon dioxide = 0.1 – 10%
- C1 – C4 HCs = 0.9 – 9%
- C5 – C6 light naphtha HCs = 0.1 – 1%

The following steps are required to derive the Acute Toxicity read across range of values for refinery stream CASRN 68377-65-6:

1. Look up the LC_{50} values for each component in Data Matrix Tables 9 and 10
2. Use the *dilution correction calculation formula* presented above to derive CV*n*, the corrected endpoint toxicity value for refinery gas *n*
3. Compare the dilution-corrected LC_{50} value ranges, and select the lowest LC50 values (i.e. most toxic LC50)
4. The read across LC50 value for CASRN 68377-65-6 is the value selected in step #3

Step 1 – LC_{50} values for neat (100%) components of the refinery gas –

Hydrogen LC50 – not applicable; an asphyxiant gas; it is not toxic unless it reaches > 80.5% of the atmosphere

Ammonia LC50 = 1590 ppm

Hydrogen sulfide LC50 = 444 ppm
Carbon monoxide LC50 = 1784 ppm
Carbon dioxide LC50 - not applicable; an asphyxiant gas; it is not toxic unless it reaches > 80.5% of the atmosphere
C1 – C4 HCs LC50 > 10,000 ppm
C5 – C6 light naphtha HCs LC50 > 1063 ppm

Step 2 – correct respective LC50 values for component dilution

Ammonia = 0.1 – 10%
- Low end of range: CV_a = 1590 ppm/0.10 = **15,900 ppm**
- High end of range: CV_a = 1590 ppm/0.001 = **1, 590,000 ppm** (> 100 % of the refinery gas)

Hydrogen sulfide = 10 – 25%
- Low end of range: CV_a = 444 ppm/0.25 = **1776** ppm
- High end of range: CV_a = 444 ppm/0.10 = **4,440** ppm

Carbon monoxide = 0.5 – 15%
- Low end of range: CV_a = 1784 ppm/0.15 = **11,893 ppm**
- High end of range: CV_a = 1784 ppm/0.005 = **356,800 ppm**

C1 – C4 HCs = 0.9 – 9%
- Low end of range: CV_a = 10,000 ppm/0.09 = **111,111 ppm**
- High end of range: CV_a = 10,000 ppm/0.009 = **1, 111,111 ppm** (> 100 % of the refinery gas)

C5 – C6 light naphtha HCs = 0.1 – 1%
- Low end of range: CV_a = 1063 ppm/0.01 = **106,300 ppm**
- High end of range: CV_a = 1063 ppm/0.001 = **1, 063,000 ppm** (> 100 % of the refinery gas)

Step 3 – compare corrected LC50 values, and selet lowest values

Hydrogen sulfide (1776 ppm – 4,440 ppm) has the lowest corrected LC50 range

Step 4 – assign LC50 read across values for CASRN 68377-65-6

LC50 range for CASRN 68477-65-6 9 = 1776 ppm – 4,440 ppm

The same four steps can be used to calculate corrected repeated-dose, developmental, and reproductive toxicity values by substituting the respective LOAEL (NOAEL) for the LC50 values in the example above. No dilution correction calculations were required for *in vitro* and *in vivo* genetic toxicity endpoints since they were designated as either *negative* or *positive.* The dilution correction calculations for each of the 62 refinery gases used to determine the constituent with the highest degree of toxicity for each endpoint and toxicity value ranges for each refinery gas are presented in Appendix 5, which is appended as a separate Excel™ spreadsheet file to this category analysis document.

7.7 Human Health Effects Conclusions

The screening level mammalian health hazards associated with Refinery Gases have been characterized by the constituents (as listed above) of each refinery gas. Refinery gas constituent hazard data were used to characterize SIDS endpoints for each of the 62 Refinery Gases in the category. To accomplish this, the endpoint value (acute LC50, reproductive toxicity NOAEL/LOAEL, etc.) for a specific gas constituent has been adjusted for dilution of each constituent in the respective refinery gas. This adjustment for the dilution of each component in a refinery gas represents the calculated concentration of the refinery gas required to reach the toxicity value (LC50, NOAEL, etc.)

corresponding to the pure substance. For example, if the LC_{50} for neat (100%) hydrogen sulfide is 444 ppm, the LC50 for a refinery gas containing 20% (wt./v) hydrogen sulfide would be 2,220 ppm; *i.e.* it would take five times more of the refinery gas containing 20% hydrogen sulfide to produce the same effect as pure hydrogen sulfide, when the refinery gas is diluted with air. In many cases, there is more than one potentially toxic constituent in a refinery gas. In those cases, the constitutent that is most toxic for a particular endpoint in an individual refinery stream is used to characterize the endpoint hazard for that stream.

This approach to correct for the concentration of the individual refinery gas constitutents to estimate the potential toxicity for mammalian endpoints makes it difficult to draw general conclusions as to which constituents are the most hazardous for human health effects of refinery gases as a category. The hazard potential for each mammalian endpoint for each of the 62 refinery gases is dependent upon each refinery gas constituent endpoint toxicity values (LC50, LOAEL, etc.) and the relative concentration of the constituent present in that gas. It should also be noted that for an individual refinery gas, the constituent characterizing toxicity may be different for different mammalian endpoints, again, being dependent upon the concentration of the different constituents in each, distinct refinery gas.

8. EXPOSURE

8.1 Overview

Refineries and gas plants create and process a variety of gaseous streams containing inorganic constituents such as hydrogen sulfide (H2S), hydrogen, carbon monoxide, ammonia, etc. Occupational exposure to these substances is limited by exposure standards and their inherent flammability hazard. These substances rarely, if ever, leave the plant without further processing to recover the valuable hydrocarbons or inorganic constituents. Some are used within the plant for process heating (burned). Because they are piped and tanked under elevated pressure and present an extreme explosion hazard should there be a release, control technologies to prevent exposure have been in place since the earliest days of the petroleum industry. All refineries and gas plants are built with pressure relief systems that include a flares to burn off excess gases. Potential releases into the environment are highly controlled by existing USEPA regulations under the Clean Air Act. There are no consumer uses for these substances and no opportunities for children to be exposed.

8.2 Product Specifications

There are no recognized product specifications for the substances in the Refinery Gases Category. These substances are typically processed to recover the hydrocarbons and hydrogen or burned as fuel gas within the plant. Some inorganic constituents are recovered as commercial products (liquid ammonia, sulfur or bisulfide from H2S) while others are routed to flares or oxidation devices (carbon monoxide).

8.3 Exposure Scenarios

Environmental Exposure
Release of Refinery Gas Category substances into the environment can occur as low level fugitive emissions from flanges and valves, a temporary release from a malfunctioning flare or other control systems, or as a catastrophic release from a ruptured pipe or tank. Emissions to air are the only likely exposure scenario. Current USEPA regulations under the Clean Air Act limit the amount of fugitive emissions, specify maximum achievable control technologies (MACT), and require planning and warnings for potential catastrophic releases.

Occupational Exposure
If a Refinery Gas Category substance is released into the air, the individual constituents separate and partition in accordance with their own individual physical-chemical properties. There are enforceable (OSHA Permissible Exposure Limits; PELs) and recommended (ACGIH) occupational exposure standards for a majority of the constituent typically found in Refinery Gas Category substances. Below is a Table of current occupational exposure standards established by OSHA (OSHA, 2009 online; HSDB 2009 online),

and the American Conference of Governmental Industrial Hygienists (ACGIH, 2008). These standards, particularly the enforceable OSHA standards, are one means that exposures to individual gas constituents are controlled; control of exposure to hazardous constituents of refinery gases additionally places a control on exposures to entire refinery gas streams that constain the hazardous constituent(s).

Table 7. OSHA and ACGIH Occupational Exposure Standards for Refinery Gas Components (8-hour Time Weighted Averages)

Category	Refinery Gases						
Component Class	Alkanes	Olefins	Alkadienes	Alkynes	> C4	Inorganics	Mercaptans
Component OSHA and/or ACGIH Occupational Exposure Standard	**Methane** **OSHA** Asphyxiant **ACGIH** 1000 ppm				**LPG** **ACGIH** 1000 ppm	**Hydrogen sulfide** **OSHA** 2 mg/m^3 **ACGIH** 10 ppm	**Methyl mercaptan** **ACGIH** 0.5 ppm
	Ethane **ACGIH** 1000 ppm	**Ethylene** **ACGIH** 200 ppm		**Ethyne**	**Gasoline Vapor** **ACGIH** 300 ppm	**Ammoni**a **OSHA** 50 ppm **ACGIH** 25 ppm	**Ethyl mercaptan** **ACGIH** 0.5 ppm
	Propane **OSHA** 1000 ppm **ACGIH** 1000 ppm	**Propylene** **ACGIH** 500 ppm	**Propa-diene**		**Benzene** **OSHA** 1 ppm **ACGIH** 1 ppm	**Hydrogen** **ACGIH** Asphyxiant	
	Butane **ACGIH** 1000 ppm	1-Butene **ACGIH** 250 ppm	**1,2 – Butadiene**		**Hexane** **OSHA** 500 ppm **ACGIH** 50 ppm	**Nitrogen** **ACGIH** Asphyxiant	
	Propane, 2-methyl **ACGIH** 1000 ppm	**2-Butene** **ACGIH** 250 ppm	**1,3-Butadiene** **OSHA** 1ppm **ACGIH** 2 ppm		**Propane** **OSHA** 1000ppm **ACGIH** 1000ppm	**Carbon dioxide** **OSHA** 5000ppm **ACGIH** 5000 ppm (by asphy-xiation)	
		Propene, 2-methyl ACGIH: 250 ppm				**Carbon monoxide** **OSHA** 50 ppm **ACGIH** 25 ppm	

Flammability is a pervasive hazard of substances in the Refinery Gases Category. Below is a Table which present the lower and upper explosive limits for key constituents of the substances in this Category. The range of the lower explosive limit is 11,000 to 50,000 ppm.

Table 8. Explosive Limits for Key Category Constituents

Fuel Gas	"Lower Explosive or Flammable Limit" (LEL/LFL) (%)	"Upper Explosive or Flammable Limit" (UEL/UFL) (%)
Benzene	1.3	7.1
Butane	1.8	8.4
Butylene	1.98	9.65
Carbon Monoxide	12	75
Ethane	3	12.4
Ethylene	2.7	36
Hydrogen	4	75
Hydrogen Sulfide	4.3	46
Isobutane	1.8	9.6
Isobutene	1.8	9
Isopentane	1.32	9.16
Gasoline	1.4	7.6
Methane	5	15
n-Hexane	1.1	7.5
Propane	2.1	10.1
Propylene	2.0	11.1

8.4 U.S. Chemical Safety and Hazard Investigation Board

The CSB is an independent federal agency charged with investigating industrial chemical accidents. The CSB conducts root cause investigations of chemical accidents at fixed industrial facilities. Root causes are usually deficiencies in safety management systems, but can be any factor that would have prevented the accident if that factor had not occurred. Other accident causes often involve equipment failures, human errors, unforeseen chemical reactions or other hazards. The agency does not issue fines or citations, but does make recommendations to plants, regulatory agencies such as the Occupational Safety and Health Administration (OSHA) and the Environmental Protection Agency (USEPA), industry organizations, and labor groups. Recent actions by the CSB that impact the Refinery Gas Category substances are listed below.

June 2006	Dangers of Propylene Cylinders in High Temperatures
January 2006	Explosion at ASCO: Dangers of Flammable Gas Accumulation
June 2003	Hazards of Nitrogen Asphyxiation

8.5 Industry Standards and Recommended Practices

The long history of petroleum refining has resulted in the development of recommended practices (RP) and standards (STD) to improve safety within the facilities. API has been a leader in developing these standards for both Upstream and Downstream operations. Listed below are groups of STDs and RPs that help ensure safe operation of the plant and reduce exposures to workers and the surrounding community.

Personnel Safety

API PERSONNEL SAFETY SET

PERSONNEL SAFETY INCLUDES THE FOLLOWING API STANDARDS: STD 2217A, RP 2016, STD 2220RP 2221, RP 54, RP 74, STD 2015

Process Safety

API PROCESS SAFETY SET

PROCESS SAFETY INCLUDES THE FOLLOWING API STANDARDS: PUBL 770, PUBL 9100, RP 751 RP 752

Safety & Fire

API SAFETY & FIRE SET

SAFETY AND FIRE - INCLUDES THE FOLLOWING API STANDARDS: 54, 74, 751, 752, 770, 2001, 2003, 2009, 2015, 2016, 2021, 2021A, 2023, 2026, 2027, 2028, 2030, 2201, 2207, 2210, 2214, 2216, 2217A 2218, 2219, 2220, 2221, 2350, 2510A, 9100

8.6 Consumer Exposure

None of the Refinery Gas Category substances are in consumer products. Several of the individual constituents in those substances are used in consumer products, i.e., butane in lighters, propane in gas grills, and natural gas (primarily methane and ethane) in stoves and heaters. Ethyl mercaptan is the odorant typically used for natural gas and propane. People are constantly exposed to small quantities of carbon monoxide, carbon dioxide, ethylene, hydrogen sulfide, and methane as they are all produced endogenously.

8.7 Exposure to Children

No direct exposure to children is anticipated.

9. Data Matrixes

Four data matrixes are presented below for this category. The first two data matrixes (Tables 9 and 10) present endpoint values for constituents of the refinery gases. Table 11 is the data matrix for Refinery Gas Category members' Physical-Chemical, Environmental Fate, and Ecotoxicology SIDS endpoints; this information is presented as technical discussions. Table 12 is the data matrix for Refinery Gas Category members' Human Health Effects SIDS endpoints.

Table 9. Inorganics: Matrix of Available Data						
SIDS Endpoint (units)	Component CASRN					
	Hydrogen 1333-74-0	Hydrogen sulfide 7783-06-4	Ammonia 7664-41-7	Nitrogen 7727-37-9	Carbon dioxide 124-38-9	Carbon monoxide 630-08-0
Physical-Chemical Properties						
Melting Point °C	-259	-85.5	-77.7	-210	-56.5	-205
Boiling Point °C	-252.8	-60.3	-33	-196	-78.5	-191.5
Vapor Pressure hPa @ 25 °C except where noted	1,653,198	20,798	10,013	1013 @ -196°C	64,395	20,664,972
Partition Coefficient	-1.14	0.45	-1.14	0.67	0.83	1.78
Water Solubility mg/L	1.62	3,980	340,000	18,100	1,480	24,582
Environmental Fate						
Photodegradation T1/2, h or d	No	T1/2 = 80.2 h	T1/2 = 16 d	No	No	Slight, T1/2 = 1559 d
Stability in Water	stable	stable	stable	stable	stable	stable
Transport and Distribution EQC Level 1	air = 100% water = <0.1% soil = <0.1% other = <0.1%	air = 100% water = <0.1% soil = <0.1% other = <0.1%	air = 88% water = 12% soil = <0.1% other = <0.1%	air = 100% water = <0.1% soil = <0.1% other = <0.1%	air = 100% water = <0.1% soil = <0.1% other = <0.1%	air = 100% water = <0.1% soil = <0.1% other = <0.1%
Biodegradation	N/A	Hydrogen sulfide can be converted to sulfur and SO_4 by sulfur-oxidizing bacteria	Ammonia undergoes nitrification by autotrophic nitrifying bacteria	N/A	N/A	Carbon monoxide is oxidized to CO2 by indigenous microbial communities
Environmental Effects						
Acute Toxicity to Fish 96-h LC_{50}, mg/L	(1)	0.007 – 0.2	0.083 – 4.6	(1)	(1)	(1)
Acute Toxicity to Aquatic Invertebrates	(1)	0.022 – 1.07	0.53 – 22.8	(1)	(1)	(1)

Table 9. Inorganics: Matrix of Available Data

SIDS Endpoint (units)	Component CASRN					
	Hydrogen 1333-74-0	Hydrogen sulfide 7783-06-4	Ammonia 7664-41-7	Nitrogen 7727-37-9	Carbon dioxide 124-38-9	Carbon monoxide 630-08-0
48-h EC_{50}, mg/L						
Toxicity to Algae 72- or 96-h EC_{50}, mg/L	(1)	no data	no data	(1)	(1)	(1)
Human Health Effects[2]						
Acute Inhalation (ppm)	Asphyxiant[3]	LC_{50} = 444 (4 hours)	LC_{50} = 4230 (1 hour) NIOSH Adj. LC_{50} = 1590 (4 hours)	asphyxiant	asphyxiant	LC_{50} = 1807 (4 hours)
Repeated-Dose (ppm)	n/a	LOAEL = 30 NOAEL = 10	LOAEL = 90 NOAEL = 50	n/a	n/a	LOAEL ≤ 100 (lowest dose tested) (monkey)
Genotoxicity, *in vitro*						
Bacterial systems	n/a	negative	negative	n/a	n/a	no data
Non-bacterial systems	n/a	equivocal (read across from methanethiol, sodium salt)	no data	n/a	n/a	no data
Genotoxicity, *in vivo*	n/a	negative (read across from methanethiol)	Negative (mouse micronuclei; ammonium ion)	n/a	n/a	no data
Reproductive Toxicity (ppm)	n/a	NOAEL ≥ 80 (highest dose tested)	NOAEL ≥ 35 (pigs; highest dose tested)	n/a	n/a	LOAEL ≤ 30 (lowest dose tested)
Developmental Toxicity (ppm)	n/a	NOAEL ≥ 80 (highest dose tested)	NOAEL ≥ 35 (pigs; highest dose tested)	n/a	n/a	LOAEL ≤ 65 (mouse) (lowest dose tested)

Table 9. Inorganics: Matrix of Available Data						
SIDS Endpoint (units)	Component CASRN					
	Hydrogen 1333-74-0	Hydrogen sulfide 7783-06-4	Ammonia 7664-41-7	Nitrogen 7727-37-9	Carbon dioxide 124-38-9	Carbon monoxide 630-08-0

n/a = not applicable; colored cell = read across data, not measured value
(1) These gases are not known to elicit toxicity to aquatic organisms. However, they may act as asphyxiants if they are released in a manner to aquatic systems whereby they displace dissolved oxygen.
(2) *in vivo* human health effects studies conducted in rats, unless otherwise noted
(3) simple asphyxiants cause suffocation by reducing pO_2 to lethal levels without toxic effects on other organ systems; SIDS endpoints are not provided

Table 10. Mercaptans, Benzene, Butadiene, C1 – C4 Hydrocarbons, and C5 – C6 Hydrocarbons: Data Matrix							
	Component CAS #						
SIDS Endpoint	Methanethiol 74-93-1	Methanethiol, sodium salt(1) 5188-0708	Ethanethiol 75-08-1	Benzene 71-43-2	1,3-Butadiene 106-99-2	Hydrocarbons C1 – C4	Hydrocarbons C5 – C6 (light naphthas)
Physical-Chemical Properties							
Melting Point °C	-123		-147.8	5.5	-109	-182 – 138	-130 - -95
Boiling Point °C	5.9		35.1	80.1	-4.5	-164 – -0.5	36 – 69
Vapor Pressure hPa @ 25°C	20,665		705	126	2,813	3,796 hPa – 350,000 hPa	201 – 685
Partition Coefficient Log Kow	0.65		1.27	2.13	1.99	1.09 – 2.8	3.4 – 3.9
Water Solubility mg/L	15,400		15,600	1790	735	24 - 61	9.5 – 38
Environmental Fate							
Photodegradation T1/2, h or d	T1/2 = 11.7 h		0.27 d	5.5 d	0.16 d	3.2 – 960 d	2 – 2.6
Stability in Water	stable		stable	stable	stable	stable	stable
Transport and Distribution EQC Level 1	air = 99% water =0.77% soil = <0.1% other = <0.1%		air = 36% water = 63% soil = 1.0% other = <0.1%	air = 99% water =0.88% soil = <0.1% other = <0.1%	air = 100% water = <0.1% soil = <0.1%	air = 100% water = <0.1% soil = <0.1%	air = 100% water = <0.1% soil = <0.1% other = <0.1%

Table 10. Mercaptans, Benzene, Butadiene, C1 – C4 Hydrocarbons, and C5 – C6 Hydrocarbons: Data Matrix							
	Component CAS #						
SIDS Endpoint	Methanethiol 74-93-1	Methanethiol, sodium salt[1] 5188-0708	Ethanethiol 75-08-1	Benzene 71-43-2	1,3-Butadiene 106-99-2	Hydrocarbons C1 – C4	Hydrocarbons C5 – C6 (light naphthas)
					other = <0.1%	other = <0.1%	
Biodegradation	inherently		inherently	inherently	inherently	inherently	inherently
Environmental Effects							
Acute Toxicity to Fish 96-h LC_{50}, mg/L	$0.5 < LC_{50} < 1.75$		1.6	5.3 – 35.7	38	11.3 – 167	3.9 – 9.5
Acute Toxicity to Aquatic Invertebrates 48-h EC_{50}, mg/L	$1.32 < EC_{50} < 2.46$		90 - 280	59.6 - 682	40	12.7 – 164	4.6 – 10.7
Toxicity to Algae 72- or 96-h EC_{50}, mg/L	no data		no data	29	25	1.3 – 95.7	3.1 – 7.0
Human Health Effects[2], [3]							
Acute Inhalation (ppm)	LC_{50} = 675 (4 hours)		LC_{50} = 2770 (4 hours; mice)	LC_{50} = 13,700 (4 hours)	LC_{50} = 129,000 (4 hours)	LC_{50} > 10,000(4 hours; highest dose tested)	LC_{50} > 1063 (4 hours; highest dose tested)
Repeated-Dose (ppm)	LOAEL = 57 NOAEL = 17		LOAEL = 57 NOAEL = 17 (read across from methanethiol)	LOAEL ≤ 10 (lowest dose tested)	LOAEL = 8000 NOAEL = 1000	LOAEL = 5000 NOAEL = 2500	LOAEL = 6625 NOAEL = 3310
Genotoxicity, *in vitro* Bacterial systems Non-bacterial systems	negative equivocal (read across both endpoints from	negative equivocal	negative positive (CHO cell SCE)	positive positive	positive positive	negative negative	negative negative

Table 10. Mercaptans, Benzene, Butadiene, C1 – C4 Hydrocarbons, and C5 – C6 Hydrocarbons: Data Matrix

	Component CAS #						
SIDS Endpoint	Methanethiol 74-93-1	Methanethiol, sodium salt[(1)] 5188-0708	Ethanethiol 75-08-1	Benzene 71-43-2	1,3-Butadiene 106-99-2	Hydrocarbons C1 – C4	Hydrocarbons C5 – C6 (light naphthas)
	methanethiol sodium salt)						
Genotoxicity, *in vivo*	negative		Negative (read across from methanethiol)	positive	positive (mice)	negative	negative
Reproductive Toxicity (ppm)	NOAEL≥ 80 (read across from hydrogen sulfide) (highest dose tested)		NOAEL ≥ 80 (read across from hydrogen sulfide) (highest dose tested)	LOAEL = 300 NOAEL = 30 (mice)	NOAEL ≥ 6000	LOAEL = 9000 NOAEL = 3000	NOAEL ≥ 6521 (highest dose tested)
Developmental Toxicity (ppm)	NOAEL ≥ 80 (read across from hydrogen sulfide) (highest dose tested)		NOAEL ≥ 80 (read across from hydrogen sulfide) (highest dose tested)	LOAEL = 20 NOAEL = 10 (mice)	NOAEL ≥ 1000	NOAEL ≥ 9000 (highest dose tested)	LOAEL = 3463 NOAEL = 680 (mice)

colored cell = read across data, not measured value

(1) Methanethiol, sodium salt is included for read across to hydrogen sulfide , methanethiol, and ethanethiol, only. Methanethiol sodium salt is not a component of Refinery Gases since it is not a gas at ambient temperatures.

(2) *in vivo* human health effects studies conducted in rats, unless otherwise noted

(3) See human health effects data matrix for each refinery gas in attached Excel spreadsheet

Table 11. Refinery Gases Physical-Chemical, Environmental Fate, and Ecotoxicology Data Matrix			
CASRN	**Physical-Chemical Endpoints of Melting Point, Boiling Point, Vapor Pressure, Partition Coefficient, and Water Solubility**	**Environmental Fate Endpoints of Photodegradation, Stability in Water, Environmental Distribution, and Biodegradation**	**Ecotoxicity Endpoints of Acute Toxicity to Fish, Invertebrates, and Algae**
All 62 Refinery Gas Streams CASRNs: 8006-20-0 thru 68989-88-8 (see Table 12 or Appendix 2 for a complete list of CASRNs)	Members of the Refinery Gases Category are mixtures of inorganic substances and organic compounds (hydrocarbons and non-hydrocarbons) having one to six carbon atoms. Proportions of these constituents in the refinery gas streams vary and may be a large or small fraction of the streams. Physical-chemical data for individual substances identified in refinery gases are provided in Section 4 of this document. Because of these streams' variable and complex make-up, no single value for these endpoints would be expected to represent the stream as a whole, but the range of values provide a general assessment of the physical-chemical nature of these refinery gas streams.	When a refinery gas stream is released into the environment, the individual constituents separate and partition to the different environmental compartments in accordance with their own individual physical-chemical properties. The ultimate fate of individual components in Refinery Gases is influenced by both abiotic and biotic processes. The environmental fate properties of the individual substances identified in refinery gases are provided in Section 5 of this document. Because these streams' variable and complex make-up, the fate characteristics of the stream would be a composite of the characteristics of the individual components. Because these exist as gases, individual components would be expected to move to the atmosphere and undergo various photochemical and transport mechanisms consistent with their specific processes.	Several of the constituents in refinery gases show substantial aquatic toxicity when exposures are controlled in laboratory experiments. To evaluate the potential for adverse effects to aquatic organisms from an environmental release of refinery gases, a conceptual exposure model was developed, and a Level 3 fugacity model was applied using the physical-chemical profiles of the individual components. Results from assessing the conceptual exposure model described in Section 6 showed that none of the constituents would partition to water in sufficient amounts to reach levels known to be acutely toxic to aquatic organisms.

Table 12. Refinery Gases Health Effects Data Matrix

CASRN	Endpoint Ranges (ppm)										
	Acute LC_{50}		Repeated-Dose[1]		*In vitro* Genotoxicity		*In vivo* Genotoxicity	Developmental Toxicity[1]		Reproductive Toxicity[1]	
	Minimum	Maximum[2]	Minimum	Maximum	Bacterial Mutagenicity	Non-bacterial		Minimum	Maximum	Minimum	Maximum
8006-20-0	6,023	9,035	333	500	Negative	Negative	Negative	217	325	100	150
	Carbon monoxide[3]		Carbon monoxide		No genotoxic constituents			Carbon monoxide		Carbon monoxide	
68308-27-0	>100%[4]	>100%	4,274	6,757	Positive	Positive	Positive	115,433	692,600	15,385	24,324
	1,3-Butadiene		C1 – C4 HCs		Contains up to 2% 1,3-butadiene[5]			C5 – C6 HCs		C1 – C4 HCs	
68476-26-6	36,140	- 364,100	2,000	20000	Negative	Equivocal	Negative	1,300	13,000	600	6,000
	Carbon Monoxide		Carbon monoxide		Contains up to 45% hydrogen sulfide			Carbon monoxide		Carbon monoxide	
68476-27-7	36,140	364,100	2,000	20,000	Negative	Negative	Negative	1,300	13,000	600	6,000
	Carbon Monxide		Carbon monoxide		No genotoxic constituents			Carbon monoxide		Carbon monoxide	
68476-28-8	18,070	361,400	1,000	20,000	Negative	Negative	Negative	650	13,000	300	6,000
	Carbon monoxide		Carbon monoxide		No genotoxic constituents			Carbon monoxide		Carbon monoxide	
68476-29-9	>100%	>100%	4,237	6,250	Positive	Positive	Positive	8,475	12,500†	15,254	22,500
	1,3-Butadiene		C1 – C4 HCs		Contains up to 2% 1,3-butadiene			NOAEL†[6]		C1 – C4 HCs[7]	

[1] Repeated-dose, developmental, and reproductive toxicity numerical ranges represent LOAEL values unless otherwise noted with the symbol †

[2] Minimum and Maximum Toxicity Values represent the concentration ranges of the constituent with the highest degree of toxicity per SIDS endpoint in the specific refinery gas; see Appendix 5 (separateEXCEL file) for calculations

[3] Refinery gas constitutent characterizing the toxicity for the respective mammalian endpoint for this CASRN; endpoint ranges are based on dilution calculations; note that the constituent characterizing toxicity may vary by endpoint for the same CASRN; see Appendix 5 (separate EXCEL file)

[4] Calculated dilution concentration was greater than 1,000,000 ppm; it would require more than 100% of the gas to cause the respective endpoint effect; note, asphyxiation would occur first at concentrations that reduce oxygen concentrations to approximately < 18% (<180,000 ppm)

[5] When benzene, 1,3-butadiene, or ethanethiol are the positive genotoxic constituents, it is unlikely that refinery gas streams containing at most 0.5 – 2 % of these components would express genotoxicity if the gases were tested directly; mutagenic concentrations of these gases would be above the lower explosive limit.

[6] '†' symbol indicates that the numerical ranges represent NOAEL values; endpoint ranges for these refinery gases are based on the highest concentration tested for the constituent with the lowest NOAEL; no developmental and/or reproductive toxicity was observed for any constituents of these gases (see Section 7.6 for further explanation)

[7] When C1 – C4 HCs was the constituent characterizing reproductive toxicity, it was assumed that 100% of the C1 – C4 HC fraction was isobutane. This is a worst case approach as other alkane gases did not produce reproductive effects when tested in studies of similar design.

Table 12. Refinery Gases Health Effects Data Matrix

CASRN	Endpoint Ranges (ppm)										
	Acute LC_{50}		Repeated-Dose[1]		*In vitro* Genotoxicity		*In vivo* Genotoxicity	Developmental Toxicity[1]		Reproductive Toxicity[1]	
	Minimum	Maximum[2]	Minimum	Maximum	Bacterial Mutagenicity	Non-bacterial		Minimum	Maximum	Minimum	Maximum
68477-65-6	1,776	4,440	120	300	Negative	Equivocal	Negative	433	13,000	200	6,000
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 45% hydrogen sulfide			Carbon monoxide		Carbon monoxide	
68477-66-7	9,035	361,400	500	10,000	Positive	Positive	Positive	325	13,000	150	6,000
	Carbon monoxide		Benzene		Contains up to 2% benzene			Carbon monoxide		Carbon monoxide	
68477-67-8	12,047	361,400	500	10,000	Positive	Positive	Positive	433	13,000	200	6,000
	Carbon monoxide		Benzene		Contains up to 2% benzene			Carbon monoxide		Carbon monoxide	
68477-68-9	9,035	361,400	500	20,000	Negative	Negative	Negative	325	13,000	150	6,000
	Carbon monoxide		Carbon monoxide		No genotoxic constituents			Carbon monoxide		Carbon monoxide	
68477-77-0	16,667	25,000	4,167	6,250	Negative	Negative	Negative	8,333	12,500†	15,000	22,500
	no lethality[1]		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68477-80-5	12,047	361,400	500	10,000	Positive	Positive	Positive	433	13,000	200	6,000
	Carbon monoxide		Benzene		Contains up to 2% benzene			Carbon monoxide		Carbon monoxide	
68477-81-6	17,094	28,571	4,274	7,143	Negative	Negative	Negative	69,260	692,600	15,385	25,714
	no lethality		C1 – C4 HCs		No genotoxic constituents			C5 – C6 HCs		C1 – C4 HCs	
68477-82-7	18,070	361,400	500	10,000	Positive	Positive	Positive	650	13,000	300	6,000
	Carbon monoxide		Benzene		Contains up to 2% benzene			Carbon monoxide		Carbon monoxide	
68477-92-9	2,960	88,800	200	6,000	Negative	Positive	Negative	533	16,000†	11,392	18,750
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 0.5% ethanethiol			NOAEL†		C1 – C4 HCs	
68477-95-2	11,100	444,000	750	30,000	Positive	Positive	Positive	173,150	> 100%	9,018	9,677
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 2% 1,3-butadiene			C5 – C6 HCs		C1 – C4 HCs	
68477-97-4	18,070	361,400	1,000	20,000	Negative	Negative	Negative	650	13,000	300	6,000
	Carbon monoxide		Carbon monoxide		No genotoxic constituents			Carbon monoxide		Carbon monoxide	

[1] Acute toxicity numerical ranges represent measured LC_{50} values from experiments where mortality was observed unless the most toxic constituent is listed as "no lethality"; "no lethality" indicates that no mortality was observed at the highest concentration of any of the individual refinery gas constituents tested; consequently this is not a true LC_{50} value range, but rather the range for the highest concentrations tested in a standard LC_{50} assay; the refinery gas constituent/constituent fraction with the lowest 'no lethality' value was selected to characterize the acute toxicity for these CASRN (see Section 7.6 for further explanation)

Table 12. Refinery Gases Health Effects Data Matrix

CASRN	Endpoint Ranges (ppm)										
	Acute LC_{50}		Repeated-Dose[1]		*In vitro* Genotoxicity		*In vivo* Genotoxicity	Developmental Toxicity[1]		Reproductive Toxicity[1]	
	Minimum	Maximum[2]	Minimum	Maximum	Bacterial Mutagenicity	Non-bacterial		Minimum	Maximum	Minimum	Maximum
68477-98-5	9,035	361,400	500	20,000	Negative	Negative	Negative	325	13,000	150	6,000
	Carbon monoxide		Carbon monoxide		No genotoxic constituents			Carbon monoxide		Carbon monoxide	
68478-00-2	4,440	88,800	300	6,000	Negative	Equivocal	Negative	650	13,000	300	6,000
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 45% hydrogen sulfide			Carbon monoxide		Carbon monoxide	
68478-01-3	12,047	361,400	667	20,000	Negative	Negative	Negative	433	13,000	200	6,000
	Carbon monoxide		Carbon monoxide		No genotoxic constituents			Carbon monoxide		Carbon monoxide	
68478-02-4	36,140	361,400	2,000	20,000	Negative	Equivocal	Negative	1,300	13,000	600	6,000
	Carbon Monxode		Carbon monoxide		Contains up to 45% hydrogen sulfide			Carbon monoxide		Carbon monoxide	
68478-03-5	8,880	88,800	600	6,000	Negative	Equivocal	Negative	1,300	13,000	600	6,000
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 45% hydrogen sulfide			Carbon monoxide		Carbon monoxide	
68478-04-6	14,800	88,800	1,000	6,000	Negative	Equivocal	Negative	2,167	13,000	1,000	6,000
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 45% hydrogen sulfide			Carbon monoxide		Carbon monoxide	
68478-05-7	8,880	88,800	500	10,000	Positive	Positive	Positive	650	13,000	300	6,000
	Hydrogen sulfide		Benzene		Contains up to 2% benzene			Carbon monoxide		Carbon monoxide	
68478-25-1	16,949	25,000	4,237	6,250	Negative	Negative	Negative	8,475	12,500†	15,254	22,500
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68478-27-3	685,000	>100%	500	10,000	Positive	Positive	Positive	1,000	20,000	15,000	300,000
	Benzene		Benzene		Contains up to 2% benzene			Benzene		Benzene	
68478-28-4	685,000	>100%	500	10,000	Positive	Positive	Positive	1,000	20,000	15,000	300,000
	Benzene		Benzene		Contains up to 2% benzene			Benzene		Benzene	
68478-29-5	10,630	106,300	4,310	8,333	Negative	Negative	Negative	34,630	346,300	15,517	30,000
	no lethality		C1 – C4 HCs		No genotoxic constituents			C5 – C6 HCs		C1 – C4 HCs	
68478-30-8	7,087	33,433	4,464	10,000	Negative	Negative	Negative	23,087	115,433	16,071	36,000
	no lethality		C1 – C4 HCs		No genotoxic constituents			C5 – C6 HCs		C1 – C4 HCs	
68513-11-1	16,949	25,000	4,237	6,250	Negative	Negative	Negative	8,475	12,500†	15,254	22,500
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68513-13-3	16,949	25,000	4,237	6.250	Negative	Negative	Negative	8,475	12,500†	15,254	22,500

Table 12. Refinery Gases Health Effects Data Matrix

CASRN	Endpoint Ranges (ppm)										
	Acute LC_{50}		Repeated-Dose[1]		*In vitro* Genotoxicity		*In vivo* Genotoxicity	Developmental Toxicity[1]		Reproductive Toxicity[1]	
	Minimum	Maximum[2]	Minimum	Maximum	Bacterial Mutagenicity	Non-bacterial		Minimum	Maximum	Minimum	Maximum
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68513-14-4	16,949	25,000	4,237	6,250	Negative	Negative	Negative	8,475	12,500†	15,254	22,500
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68513-16-6	88,800	444,000	2,551	2,809	Negative	Equivocal	Negative	5,102	5,618†	9,184	10,112
	Hydrogen sulfide		C1 – C4 HCs		Contains up to 45% hydrogen sulfide			NOAEL†		C1 – C4 HCs	
68513-18-8	20,408	40,000	5,102	10,000	Negative	Negative	Negative	10,204	20,000†	18,367	36,000
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68513-19-9	20,408	40,000	5,102	10,000	Negative	Negative	Negative	10,204	20,000†	18,367	36,000
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68513-68-8	>100%	>100%	1,000	20,000	Positive	Positive	Positive	2,000	40,000	9,474	11,250
	Benzene		Benzene		Contains up to 2% benzene			Benzene		C1 – C4 HCs	
68527-13-9	987	1,269	67	86	Negative	Equivocal	Negative	650	6,500	300	3,000
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 45% hydrogen sulfide			Carbon monoxide		Carbon monoxide	
68527-14-0	12,500	16,667	3,125	4,167	Negative	Negative	Negative	6,250	8,333†	11,250	15,000
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68527-15-1	9,035	361,400	500	20,000	Negative	Negative	Negative	325	13,000	150	6,000
	Carbon monoxide		Carbon monoxide		No genotoxic constituents			Carbon monoxide		Carbon monoxide	
68602-82-4	18,070	361,400	1,000	10,000	Positive	Positive	Positive	650	13,000	300	6,000
	Carbon monoxide		Benzene		Contains up to 2% benzene			Carbon monxide		Carbon monoxide	
68602-84-6	22,222	28,571	5,556	7,143	Negative	Negative	Negative	11,111	14,288†	20,000	25,714
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68607-11-4	22,727	47,619	5,682	11,905	Negative	Negative	Negative	11,364	14,288†	20,455	25,714
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68783-05-1	1,480	2,220	100	150	Negative	Equivocal	Negative	58	78†	58	78†
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 45% hydrogen sulfide			NOAEL†		NOAEL†	
68783-06-2	16,949	25,000	4,237	6,250	Negative	Negative	Negative	8,475	12,500†	15,254	22,500
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	

Table 12. Refinery Gases Health Effects Data Matrix

CASRN	Endpoint Ranges (ppm)										
	Acute LC_{50}		Repeated-Dose[1]		*In vitro* Genotoxicity		*In vivo* Genotoxicity	Developmental Toxicity[1]		Reproductive Toxicity[1]	
	Minimum	Maximum[2]	Minimum	Maximum	Bacterial Mutagenicity	Non-bacterial		Minimum	Maximum	Minimum	Maximum
68783-07-3	11,100	444,000	750	30,000	Positive	Positive	Positive	1,300	13,000	600	6,000
	hydrogen sulfide		Hydrogen sulfide		Contains up to 2% 1,3-butadiene			Carbon monoxide		Carbon monoxide	
68783-62-0	1,100	444,000	75	30,000	Positive	Positive	Positive	1,300	13,000	600	6,000
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 2% 1,3-butadiene			Carbon monoxide		Carbon monoxide	
68814-47-1	1,269	2,220	86	150	Positive	Positive	Positive	34,630	346,300	18,367	36,000
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 2% 1,3-butadiene			C5 – C6 HCs		C1 – C4 HCs	
68814-67-5	16,949	25,000	4,237	6,250	Negative	Negative	Negative	8,475	12,500†	15,254	22,500
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68814-90-4	16,949	25,000	4,237	6,250	Negative	Negative	Negative	8,475	12,500†	15,254	22,500
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68911-58-0	8,880	88,800	600	6,000	Negative	Equivocal	Negative	1,300	13,000	600	6,000
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 45% hydrogen sulfide			Carbon monoxide		Carbon monoxide	
68911-59-1	36,140	361,400	2,000	20,000	Negative	Negative	Negative	1,300	13,000	600	6,000
	Carbon monxide		Carbon monoxide		No genotoxic constituents			Carbon monoxide		Carbon monoxide	
68919-01-7	987	1,776	67	120	Negative	Equivocal	Negative	178	320†	16,364	22,500
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 45% hydrogen sulfide			NOAEL†		C1 – C4 HCs	
68919-02-8	2,960	44,400	200	3,000	Positive	Positive	Positive	34,630	346,300	20,455	36,000
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 2% 1,3-butadiene			C5 – C6 HCs		C1 – C4 HCs	
68919-03-9	18,519	25,000	4,630	6,250	Negative	Negative	Negative	9,259	12,500†	16,667	22,500
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68919-04-0	2,960	44,400	200	3,000	Negative	Equivocal	Negative	34,630	346,300	20,455	36,000
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 45% hydrogen sulfide			C5 – C6 HCs		C1 – C4 HCs	
68919-07-3	16,949	25,000	4,237	6,250	Negative	Negative	Negative	8,475	12,500†	15,254	22,500
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68919-08-4	222,000	888,000	4,630	10,000	Negative	Equivocal	Negative	23,087	69,260	16,667	36,000
	Hydrogen sulfide		C1 – C4 HCs		Contains up to 45% hydrogen sulfide			C5 – C6 HCs		C1 – C4 HCs	
68919-12-0	18,519	25,000	4,630	6.250	Negative	Negative	Negative	9,259	12,500†	16,667	22,500

Table 12. Refinery Gases Health Effects Data Matrix

CASRN	Endpoint Ranges (ppm)										
	Acute LC_{50}		Repeated-Dose[1]		*In vitro* Genotoxicity		*In vivo* Genotoxicity	Developmental Toxicity[1]		Reproductive Toxicity[1]	
	Minimum	Maximum[2]	Minimum	Maximum	Bacterial Mutagenicity	Non-bacterial		Minimum	Maximum	Minimum	Maximum
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68952-79-4	16,949	25,000	4,237	6,250	Negative	Negative	Negative	8,475	12,500†	15,254	22,500
	no lethality		C1 – C4 HCs		No genotoxic constituents			NOAEL†		C1 – C4 HCs	
68952-80-7	>100%	>100%	4,310	8,333	Positive	Positive	Positive	34,630	364,300	15,517	30,000
	1,3-Butadiene		C1 – C4 HCs		Contains up to 2% 1,3-butadiene			C5 – C6 HCs		C1 – C4 HCs	
68955-33-9	>100%	>100%	4,237	6,250	Positive	Positive	Positive	8,475	12,500†	15,254	22,500
	1,3-Butadiene		C1 – C4 HCs		Contains up to 2% 1,3-butadiene			NOAEL†		C1 – C4 HCs	
68989-88-8	4,440	88,800	300	6,000	Positive	Positive	Positive	650	13,000	300	6,000
	Hydrogen sulfide		Hydrogen sulfide		Contains up to 2% benzene			Carbon monoxide		Carbon monoxide	

10. Refinery Gases Category Analysis Conclusions

All Refinery Gases Category members contain one or more inorganic compounds in addition to hydrocarbons as listed in the stream TSCA definitions. The inorganic components of the Refinery Gases are more toxic than the C1 – C4 and C5 – C6 hydrocarbon components to both mammalian and aquatic organisms. Unlike other petroleum product categories (*e.g.* gasoline, diesel fuel, lubricating oils, etc.), the inorganic and hydrocarbon constituents of refinery gases can be evaluated for hazard individually to then predict the screening level hazard of the Refinery Gases Category members. The 12 refinery gas constituents identified to characterize refinery gas category member hazard are:

- Inorganic Gases
    - Ammonia
    - Carbon Monoxide
    - Ethyl mercaptan
    - Hydrogen sulfide
    - Methyl mercaptan
- Hydrocarbon Gases
    - Benzene
    - 1,3-Butadiene
    - C1 – C4 Hydrocarbons
    - C5 – C6 Hydrocarbons
- Asphyxiant Gases
    - Carbon dioxide
    - Hydrogen gas
    - Nitrogen gas

The different components making up refinery gases typically have extremely low melting and boiling points. They also have high vapor pressures and low octanol/water partition coefficients. The aqueous solubilities of these substances vary, and range from low parts per million (hydrogen gas) to several hundred thousand parts per million (ammonia). The environmental fate characteristics of refinery gases are governed by these physical-chemical attributes. Components of the refinery gas streams will partition to the air, and depending on the specific constituent, photodegradation reactions may be either an important fate process or have little influence. Some of the gases are chemically stable and may be lost to the atmosphere or simply become involved in the environmental cycling of their atoms. Some show substantial water solubility, but their volatility eventually causes these gases to enter the atmosphere.

Several of the inorganic constituents in refinery gases are highly hazardous to aquatic organisms as demonstrated in laboratory toxicity tests where exposure concentrations can be maintained over time. Hydrogen sulfide was the most toxic constituent to fish and invertebrates. Ammonia also is a relative toxic component in refinery gases. While acute LC/EC50 values were typically < 1 mg/L for these constituents, the hydrocarbon components in refinery gases were generally less toxic. Acute LC/EC50 values for this constituent group ranged roughly from 1 to 100 mg/L. Although the LC/EC50 data for the individual gases illustrate the potential toxicity to aquatic organisms, aqueous concentrations from atmospheric releases of these gases would likely not persist for a sufficient duration to elicit toxicity. Based on a simple conceptual exposure model analysis, it was shown that atmospheric emissions of refinery gases did not result in acutely toxic concentrations in adjacent water bodies because such emissions will tend to remain in the atmosphere.

The mammalian health hazards associated with Refinery Gases have been characterized by the 12 constituents of the refinery gases. The mammalian SIDS endpoint ranges for potential toxicity in the 62 refinery gases are conservative because interpretation of hazard study data for the constituents in refinery gases has been conservative on the side of over-predicting the potential hazard. Refinery gas constituent hazard data were used to characterize SIDS endpoints for each of the 62 Refinery Gases in the category. To accomplish this, the endpoint value (acute LC50, reproductive toxicity NOAEL/LOAEL, etc.) for a specific gas constituent has been adjusted for dilution of each constituent in the respective refinery gas. This adjustment for the dilution of each component in a refinery gas represents the calculated

concentration of the refinery gas required to reach the toxicity value (LC_{50}, NOAEL, etc.) corresponding to the pure substance. For example, if the LC_{50} for neat (100%) hydrogen sulfide is 444 ppm, the LC50 for a refinery gas containing 20% (wt./v) hydrogen sulfide would be 2,220 ppm; *i.e.* it would take five times more of the refinery gas containing 20% hydrogen sulfide to produce the same effect as pure hydrogen sulfide, when the refinery gas is diluted with air. In many cases, there is more than one potentially toxic constituent in a refinery gas. In those cases, the constitutent that is most toxic for a particular endpoint in an individual refinery stream is used to characterize the endpoint hazard for that stream. A more detailed explanation with examples of these calculations, along with the calculations for each of the 62 refinery gases used to determine which constituent to use to characterize mammalian SIDS endpoint-specific hazard for each gas (listed in the Human Health Effects Data Matrix, Table 12) is presented in the body of the document.

This approach to correct for the concentration of the individual refinery gas constitutents to estimate the potential toxicity for mammalian endpoints makes it difficult to draw general conclusions as to which constituents are the most hazardous for human health effects of refinery gases as a category. The hazard potential for each mammalian endpoint for each of the 62 refinery gases is dependent upon each refinery gas constituent endpoint toxicity values (LC50, LOAEL, etc.) and the relative concentration of the constituent present in that gas. It should also be noted that for an individual refinery gas, the constituent characterizing toxicity may be different for different mammalian endpoints, again, being dependent upon the concentration of the different constituents in each, distinct refinery gas.

The human health endpoint ranges of potential toxicity for each of the 62 Refinery Gases Category members are considered adequate for screening level hazard characterization and subsequent screening level risk assessments to be conducted using this information.

11. REFERENCES

Abraham M.H. et al. 1994. J. Pharm. Sci. 83:1085-100. [Cited in: NLM (U.S. National Library of Medicine). 2005. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

ACC (American Chemistry Council). 2004. Category Summary for Crude Butadiene C4 Category. Prepared by Olefins Panel of the American Chemistry Council as part of the U.S. High Production Volume (HPV) Chemical Program. American Chemistry Council, Washington, DC.

ACGIH. 2008. American Conference of Governmental Industrial Hygienists: TLVs® and BEIs®. Pages 72; 86 – 91.

AIHA (American Industrial Hygiene Association). 2000. Risk Assessment Principles for the Industrial Hygienist. American Industrial Hygiene Association Press, Fairfax, VA.

Alden, C.L., Kenewa, R.L., Redder, G., and Stone, L.C. 1984. The pathogenesis of the nephrotoxicity of volatile hydrocarbons in male rats. Chapter VIII in Renal Effects of Petroleum Hydrocarbons, Mehlman et al., Eds. Princeton Scientific Publishers, Princeton, NJ. pp. 107-120.

API (American Petroleum Institute) 1977. Mutagenicity evaluation of unleaded gasoline (L5178Y Mouse lymphoma assay and Ames test). API Rpt #28-30173. Washington, DC. [report includes single ip dose *in vivo* cytogenetic assay]

API (American Petroleum Institute) 1984. Acute inhalation toxicity evaluation of a petroleum derived hydrocarbon in rats. API 83-05 Full range catalytic reformed naphtha. API Rpt. #31-30681. Washington, DC

API (American Petroleum Institute) 1985. Acute oral toxicity study in rats, acute dermal toxicity study in rabbits, primary dermal irritation study in rabbits, primary eye irritation study in rabbits, API 83-05 Full range catalytic reformed naphtha (CAS #68955-35-1). API Rpt #32-31474, Washington, DC.

API (American Petroleum Institute) 1987a. Acute inhalation toxicity evaluation of a petroleum derived hydrocarbon in rats. API 83-19 Light alkylate naphtha. API Rpt. #34-30636. Washington, DC

API (American Petroleum Institute) 1987b. Acute inhalation toxicity evaluation of a petroleum derived hydrocarbon in rats. API 83-20 Light catalytic cracked naphtha. API Rpt. #34-32777. Washington, DC

API (American Petroleum Institute) 1987c. Acute inhalation toxicity evaluation of a petroleum derived hydrocarbon in rats. API 81-08 Sweetened naphtha. API Rpt #33-31827. Washington, DC

API (American Petroleum Institute). 2001. Petroleum Gases Test Plan. Submitted to the U.S. EPA by The Petroleum HPV Testing Group, American Petroleum Institute, Washington, DC.

API (American Petroleum Institute) 2005a. Baseline Gasoline Vapor Condensate. A 13 week Whole Body Inhalation Toxicity Study in Rats with Neurotoxicity Assessments and 4-week In Vivo Genotoxicty and Immunotoxicity Assessments. HLS Study No. 00-6125. Huntingdon Life Sciences Laboratories, East Millstone, NJ

API (American Petroleum Institute) 2005b. Baseline Gasoline Vapor Condensate. Micronucleus Assay in a 13 week Whole Body Inhalation Toxicity Study in Rats with Neurotoxicity Assessments and 4-week In Vivo Genotoxicity and Immunotoxicity Assessments. HLS Study No. 00-6125, Vol IV, Appendix X. Huntingdon Life Sciences Laboratories, East Millstone, NJ and Huntingdon Eye Research Center, Suffolk, UK

API (American Petroleum Institute) 2005c. Baseline Gasoline Vapor Condensate. Sister Chromatid Exchange Assay in a 13 week Whole Body Inhalation Toxicity Study in Rats with Neurotoxicity Assessments and 4-week In Vivo Genotoxicity and Immunotoxicity Assessments. HLS Study No. 00-6125, Vo. IV, Appendix Y. Huntingdon Life Sciences Laboratories, East Millstone, NJ and BioReliance Laboratories, Rockville, MD

API (American Petroleum Institute). 2008a. Gasoline Blending Streams Category Analysis Document. Submitted to the USEPA by API Petroleum HPV Testing Group, Consortium Registration # 1100997.

API (American Petroleum Institute) 2008b. Baseline Gasoline Vapor Condensate. Whole-Body Inhalation Developmental Toxicity Study in Rats with Baseline Gasoline Vapor Condensate. . EMBSL #MRD-00-695:169534. ExxonMobil Biomedical Sciences Inc., Annandale, NJ

API (American Petroleum Institute) 2008c. Baseline Gasoline Vapor Condensate, A 2-Generation Whole Body Inhalation Reproductive Study in Rats. HLS Study No. 00-4207. Huntingdon Life Sciences Laboratories, East Millstone, NJ

API (American Petroleum Institute) 2009. Baseline Gasoline Vapor Condensate. Whole-Body Inhalation Developmental Toxicity Study in Mice with Baseline Gasoline Vapor Condensate. EMBSL #MRD-00-695:169534M. ExxonMobil Biomedical Sciences Inc., Annandale, NJ

Arce GT., DR Vincent, MJ Cunningham, WN Choy and AM Sarrif. 1990. *In vitro* and *in vivo* genotoxicity of 1,3-butadiene and metabolites. Environ. Health Perspect. 86:75-8.

Arts, J.H.E. 1992. Acute (4-hour) inhalation toxicity study of butene-2 in rats. Report No. V92.183/352130. TNO

Atkinson, R. 1989. J. Phys. Chem. Ref. Data. Monograph No. 1. [Cited in: NLM (U.S. National Library of Medicine). 2005. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

ATSDR (Agency for Toxic Substances and Disease Registry). 2004. Toxicological Profile for Ammonia. http://www.atsdr.cdc.gov/toxprofiles/tp126.html#bookmark07

ATSDR. 2006. Toxicological Profile for Hydrogen Sulfide. http://www.atsdr.cdc.gov/toxprofiles/tp114.html

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.

Aviado, D.M., S. Zakhari, and T. Watanabe. 1977. Part 2: Hydrocarbon Propellants, In Non-fluorinated Propellants and Solvents for Aerosols. CRC Press, Inc., West Palm Beach, Fla.

Bartholomew, G.W., and M. Alexander. 1979. Microbial Metabolism of Carbon Monoxide in Culture and In Soil. App. Environ. Microbiol. 37(5):932-937.

BASF AG, Abteilung Analytik; unveroeefentlichte Untersuchung (BRU 92.004). 1992a.[cited in ECB (European Chemicals Bureau). 2000. IUCLID Dataset for Ammonia, CAS No. 7664-41-7. European Commission, Brussels, Belgium]

BASF AG, Abteilung Analytik; unveroeffentlichte Untersuchung (BRU 92.003). 1992b. [cited in ECB (European Chemicals Bureau). 2000. IUCLID Dataset for Hydrogen Sulphide, CAS No. 7783-06-4. European Commission, Brussels, Belgium]

BIBRA. 1995. Toxicology Profile: Ammonia. BIBRA International.

Boikess, R.S., and E. Edelson. 1978. Chemical Principles. Harper and Row Publishers, New York, New York. 742 p.

Brenneman, KA, James, RA, Gross, EA, Dorman, DC. (2000) Olfactory loss in adult male CD rats following inhalation exposure to hydrogen sulfide. Toxicologic Pathology 28(2): 326-333.

Brooke, L. 1987. Acute Test Comparisons with Fathead Minnows and Acute Tests with an Amphipod and a Cladoceran. Centre for Lake Superior Environmental Studies, University of Wisconsin – Superior, Wisconsin. 24 p.

Budavari, S. (ed.). 1996. The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Merck and Co., Inc., Whitehouse Station, NJ. [cited in NLM (U.S. National Library of Medicine). Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

CIIT (Chemical Industry Institute of Toxicology). 1983a. 90-Day vapor inhalation toxicity study of hydrogen sulfide in B6C3F1 mice. EPA/OTS 0883-0255.

CIIT (Chemical Industry Institute of Toxicology). 1983b. 90-Day vapor inhalation toxicity study of hydrogen sulfide in Fischer-344 rats. EPA/OTS 0883-0255.

CIIT (Chemical Industry Institute of Toxicology). 1983c. 90-Day vapor inhalation toxicity study of hydrogen sulfide in Sprague-Dawley rats. EPA/OTS 0883-0255.

Clark DG and DJ Tinson (1982) Acute inhalation toxicity of some halogenated and non-halongenated hydrocarbons. Human Toxicol 1:239-247.

Clement Associates, Inc. 1990. Health Effects Assessment for Ammonia. Prepared for The Fertilizer Institute, Washington, D.C.

Cochrane, JE and TR Skopek. 1994. Mutagenicity of butadiene and its epoxide metabolites: I. Mutagenic potential of 1,2-epoxybutene, 1,2,3,4-diepoxybutane and 3,4-epoxy-1,2-butanediol in cultured human lymphoblasts. *Carcinogenesis* 15: 713-17.

Csanady G, Guengerich F and Bond J (1992). Comparison of the biotransformation of l,3-butadiene and its metabolite, butadiene monoepoxide, by hepatic and pulmonary tissues from humans, rats and mice. Carcinogenesis **13**, 1143-1153.

Daubert, T.E., and R.P. Danner. 1989. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Taylor and Francis, Washington, D.C. [cited in: NLM (U.S. National Library of Medicine). Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

DeBias DA, CM Banerjee, NC Birkhead, WV Harrer, LA Kazal.1973. Effects of carbon monoxide inhalation on ventricular fibrillation.Arch Environ Health 27: 161-167

DeGraeve, G.M., R.G. Elder, D.C. Woods, and H.L. Bergman. 1982. Effects of Naphthalene and Benzene on Fathead Minnows and Rainbow Trout. Arch. Environ. Contam. Toxicol. 11(4):487-490.

Diaz, J., Tornel, P.L., and Martinez, P. 1995. Reference intervals for blood ammonia in health subjects determined by microdiffusion. Clin. Chem., 41(7):1048.

Diekman, M.A., Scheidt, A.B., Sutton, A.L., Green, M.L., Clapper, J.A., Kelly, D.T., and Van Alstine, W.G. 1993. Growth and reproductive performance, during exposure to ammonia, of gilts afflicted with pneumonia and atrophic rhinitis. Am. J. Vet. Res. 54(12):2128-2131.

Dorman, D.C., Struve, M.F., Gross, E.A., and Brenneman, K.A. (2004). Respiratory tract toxicity of inhaled hydrogen sulfide in Fischer-344 rats, Sprague-Dawley rats, and B6C3F1 mice following subchronic (90-day) exposure. Toxicol. Appl. Pharmacol. 198(1):29-39.

Dorman, DC; Brenneman, K A; Struve, MF; Miller, KL; James, RA; Marshall, MW; Foster, P M. (2000) Fertility and developmental neurotoxicity effects of inhaled hydrogen sulfide in Sprague-Dawley rats. Neurotoxicol Teratol 22:71-84.

Drew RT, Fouts JR. 1974. The lack of effects of pretreatment with phenobarbital and chlorpromazine on the acute toxicity of benzene in rats. Toxicol Appl Pharmacol 27:183-193.

Eastmond, D.A., G.M. Booth, and M.L. Lee. 1984. Toxicity, Accumulation, and Elimination of Polycyclic Aromatic Sulfur Heterocycles in Daphnia magna. Arch. Environ. Contam.Toxicol. 13(1):105-111.

ECB (European Chemicals Bureau). 2000. IUCLID Dataset for Hydrogen Sulphide (CAS 7783-06-4). Brussels, Belguim.

ELF Atochem. 1992. Sodium methyl mercaptide. Reverse mutation assay by the Amestest. CIT Report no. 9102 MO, 7 August 1992.

ELF Atochem. 1995. In vitro mammalian chromosome aberration test in cultured human lymphocytes with sodium methylmercaptide. CIT report no. 12086 MLH, 15 November 1995.

Elf Atochem North America. 1997. Bone marrow micronucleus assay in male and female Swiss-Webster mice following acute nose-only inhalation exposure to methyl mercaptan. SRI International report no. M020-95, 8 January 1997.

Elf Atochem S.A. 2000. Methyl Mercaptan 33% sodium: Acute toxicity to daphnias. Centre d'Application de Levallois study no. 604/99/A. [Cited in HPVIS database for methanethiol sodium salt]

Erexson, G.L., Wilmer, J.L., Steinhagen, W.H., Kilgerman, A.D. 1986. Induction of Cytogenetic Damage in Rodents after Short-Term Inhalation of Benzene. Environ. Mutagen. 8:29-40.

Fairchild, EJ and Stokinger, HE (1958) Toxicologic studies on organic sulfur compounds. I. Acute toxicity of some aliphatic and aromatic thiols (Mercaptans). Am. Ind. Hyg. Assoc. J. 19:171-189.

Fuerst, R. and S. Stephens. 1970. Studies of Effects of Gases and Gamma Irradiation on Neurospora crassa. Dev. Ind. Microbiol. 11:301-310.

Fung, D.K., and P.H. Bewick. 1980. Short-Term Toxicity of Aqueous Hydrogen Sulfide to Representative Fish Species of Lake Huron. In: Eaton, J.G., P.R. Parrish, and A.C. Hendricks (Eds.), Aquatic Toxicology and Hazard Assessment, 3rd Symposium, ASTM STP 707, Philadephia, PA.

Galassi, SM, Mingazzini, L, . Vigano, D, Cesaeeo, and ML Tosato. 1988. Approaches to Modeling the Toxic Responses of Aquatic Organisms to Aromatic Hydrocarbons. Ecotoxicol. Environ. Saf. 16(2):158-169.

Galvin, J.B., and F. Marashi. 1999. 2-Methylbutane (Isobutane). J. of Toxicol. and Environ. Health, Part A. 58:23-33.

Garvey, D.J., and L.D. Longo. 1979. Chronic low level maternal carbon monoxide exposure and fetal growth and development. Biol. Reprod. 19:8-14.

Glatt H, Padykula R, Berchtold GA, et al. (1989) Multiple activation pathways of benzene leading to products with varying genotoxic characteristics. Environ Health Perspect 82:81-89.

Green JD, Snyder CA, LoBue J, et al. (1981a) Acute and chronic dose/response effects of inhaled benzene on multipotential hematopoietic stem (CFU-S) and granulocyte/macrophage progenitor (GMCFU-C) cells in CD-1 mice. Toxicol Appl Pharmacol 58:492-503.

Green JD, Snyder CA, LoBue J, et al. (1981b) Acute and chronic dose/response effect of benzene inhalation on the peripheral blood, bone marrow, and spleen cell of CD-1 male mice. Toxicol Appl Pharmacol 59:204-214.

Hansch, C., A. Leo, and D. Hoekman. 1995. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. American Chemical Society, Washington, DC. [Cited in: NLM (U.S. National Library of Medicine). 2008. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

Harris, J.C. 1982a. 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 Co., NY.

Harris, J.C. 1982b. 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 Co., NY.

Hazardous Substances Data Bank (HSDB)**.** 2009. Available at http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

Hayashi ,M, Kishi, M, Sofuni, T and M Ishidate Jr. 1988. Micronucleus test in mice on 39 food additives and eight miscellaneous chemicals. Food. Chem.Toxicol. 26, 487-500.

Haydu, E.P. et al, 1952.The effect of kraft mill waste components on certain salmonoid fishes of the Pacific Northwest. TAPPI, 35(12), 545-549. [Cited in: HPVIS database for methanethiol]

Hazleton Laboratories, Inc. 1984a (for Phillips Petroleum Co.). Salmonella typhimurium mammalian microsome plate incorporation assay with ethyl mercaptan, May 5, 1983. Project No. 652-145.

Hazleton Laboratories, Inc. 1984b (for Phillips Petroleum Co.). *In vitro* sister chromatid exchange in Chinese hamster ovary cells. ethyl mercaptan. Final Report. December 11, 1984. OTS0571888.

Henderson R, Thornton-Manning J, Bechtold W and Dahl A (1996). Metabolism of l,3-butadiene: species differences. Toxicology **113**, 17-22.

Himmelstein, MW, JF Acquavella, L Recio, *et al.* 1997.Toxicology and epidemiology of 1,3-butadiene, *Crit Rev Toxicol* 27: 1-108.

Hine J. and P.K. Mookerjee. 1975. J. Org. Chem. 40: 292-8. [Cited in: NLM (U.S. National Library of Medicine). 2005. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

HLS (Huntinton Life Sciences), 2008. Isobutane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4244.

Kapeghian, J.C., H.H.Mincer, A.B. Jones, A.J. Verlangieri, and I.W. Waters. 1982. Acute inhalation toxicity of ammonia in mice. Bull. Environ. Contam. Toxicol 29(3)371-378.

Keller, KA., Snyder, CA. 1988. Mice exposed in utero to 20 ppm benzene exhibit altered numbers of recognizable hematopoietic cells up to seven weeks after exposure. Fundam. Appl. Toxicol. 10: 224-232.

Khan, S.H. Ward, C.O. 1985. Micronucleus test of Gulftene® 4 [1-butene]. Unpublished report # 84-2113 by Gulf Life Sciences Center for Gulf Oil Chemicals Co.

Kiene, R.P., and D.G. Capone. 1988. Microb. Ecol. 15: 275-91. [Cited in: NLM (U.S. National Library of Medicine). 2005. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

Kirk-Othmer Encyclopedia of Chemical Technology. 1991. 4th ed. Volumes 1. John Wiley and Sons, New York, NY. p. V23 277. [Cited in: NLM (U.S. National Library of Medicine). 2008. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

Kligerman, AD and Y Hu. 2007. Some insights into the mode of action of butadiene by examining the genotoxicity of its metabolites. *Chem Biol Inter* 166: 132-139.

Kuna, R.A., Nicolich, M.J., Schroeder, R.E., Rusch, G.M. (1992): A female rat fertility study with inhaled benzene. Journal of the American College of Toxicology 3: 275-282

Lide, D.R. (ed.). 1994 – 1995. CRC Handbook of Chemistry and Physics. 75th ed. CRC Press Inc., Boca Raton, Fl. p. 4-50. [Cited in: NLM (U.S. National Library of Medicine). 2008. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

Lide, D.R., and G.W.A. Milne (eds.). 1994. Handbook of Data on Organic Compounds. Volume I. 3rd ed. CRC Press, Inc. Boca Raton ,FL. p. V3: 2660. [Cited in: NLM (U.S. National Library of Medicine). 2006. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov

Lomans, B.P., H.J.M. Op den Camp, A. Pol, and G. D. Vogels. 1999. Anaerobic Versus Aerobic Degradation of Dimethyl Sulfide and Methanethiol in Anoxic Freshwater Sediments. App. Environ. Microbiol. 65(2):438-443.

Maas, J.L. 1990. Toxicity research with thiourea. Laboratory for ecotoxicology, Institute for Inland Water Management and Waste Water Treatment, Report No. AOCE: 4 p (DUT). [Cited in: ECB, 2000]

Mackay, D., A. Di Guardo, S. Paterson, and C. E. Cowan. 1996. Evaluating the Environmental Fate of a Variety of Types of Chemicals Using the EQC Model. Environ. Toxicol. Chem. 15:1627-1637.

Mackay, D., DiGuardo, A. Paterson, S., and Cowan, C. 1997. EQC Model, Version. 1.01, 1997, available from the Environmental Modelling Centre, Trent University, Canada.

MacLean, M.M., and K.G. Doe. 1989. The Comparative Toxicity of Crude and Refined Oils to Daphnia magna and Artemia. Environment Canada, EE-111, Dartmouth, Nova Scotia :64 p.

May, W.E. et al. 1983. J. Chem. Ref. Data 28: 197-0200. [Cited in: NLM (U.S. National Library of Medicine). 2005. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

McAuliffe, C. 1966. J. Phys. Chem. 70: 1267-75. [Cited in: NLM (U.S. National Library of Medicine). 2005. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

McConnell, J.C. 1973. Atmospheric Ammonia. J. Geophys. Res. 78:7812-7821. [as cited in NRC, 1979]

McKee, R.H. et al (2000) Assessment in rats of the reproductive toxicity of gasoline from a gasoline vapor recovery unit. Reproductive Toxicology 14, 4, 337-353

McManus, N. 1999. Safety and Health in Confined Spaces. Lewis Publishers, Boca Raton, FL.

Morimoto K (1983) Induction of sister chromatid exchanges and cell division delays in human lymphocytes by microsomal activation of benzene. Cancer Res 43:1330-1334.

Morrissey R, Schwetz B, Hackett P, Sikov M, Hardin B, McClanahan B, Decker J and Mast T .1990. Overview of reproductive and developmental toxicity studies of 1,3-butadiene in rodents. Environ. Health Perspect. **86**, 79-84.

MTC (Mercaptans/Thiols Council). 2001. Methyl Mercaptan (CAS 74-93-1) [and] Methyl Mercaptide (CAS 5188-07-8) High Production Volume Challenge Program Test Plan. Submitted to the USEPA December 4, 2001 by the Mercaptan/Thiols Council, Leesburg, VA. Pages 6-7, 12-18. Available at http://iaspub.epa.gov/oppthpv/document_api.download?FILE=c13333tp.pdf).

NIOSH. 1980 U.S. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH.

NIOSH. 1987 U.S. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.

NIOSH. 1994. Documentation for immediately Dangerous to Life or Health Concentrations (IDLH): Introduction.

NLM (U.S. National Library of Medicine). 2006. Ethyl Mercaptan, Hazardous Substance Data Bank Number 814. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov

NRC (National Research Council). 1979. Ammonia. Subcommittee on Ammonia, Committee on Medical and Biologic Effects of Environmental Pollutants, Division of Medical Sciences, Assembly of Life Sciences, National Research Council. University Park Press, Baltimore, Maryland. 384 p.

NRC (National Research Council). 2007. Acute Exposure Guideline Levels for Selected Airbourne Chemicals, pp. 58-114. Available at: http://www.nap.edu/catalog/12018.html.

NRCC (National Research Council Canada). 1981. Hydrogen Sulfide in the Atmospheric Environment. NRCC Report No. 18467. [Cited in: European Chemicals Bureau ESIS Database, http://ecb.jrc.ec.europa.eu/esis/]

O'Brien, W.E., and L.R. Brown. 1967. The Catabolism of Isobutane and other Alkanes by a Member of the Genus Mycobacterium. Dev. Ind. Microbiol. 9:389-393.

OECD (Organization for Economic Cooperation and Development). 2007. Manual for Investigation of HPV Chemicals. www URL: http://www.oecd.org/document/7/0,3343,en_2649_201185_1947463_1_1_1_1,00.html

Ohe S. 1976. Computer Aided Data Book of Vapor Pressure. Data Book Publ. Co, Tokyo, Japan. [cited in NLM (U.S. National Library of Medicine). 2008. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

O'Neil, M.J. (ed.). 2001. The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. 13th Edition. Merck and Co., Inc., Whitehouse Station, NJ. [Cited in: NLM (U.S. National Library of Medicine). 2005. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

OSHA. 2009. PEL Project Documentation and Standard Lists by Chemical Name. Available at http://www.cdc.gov/niosh/pel88/npelname.html; http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=9992; and http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=9993

Owen PE and JR Glaister. 1990. Inhalation toxicity and carcinogenicity of 1,3-butadiene in Sprague-Dawley rats. *Environ Health Persp*. **86;** 19-25.

Perry, R.A., A. Atkinson, and J.N. Pitts, Jr. 1976. Rate Constants for the Reactions OH + H2S → SH and OH + NH3 → H2O + NH2 over the Temperature Range 297 – 427°K. J. Chem. Phys. 64:3237-3239. [as cited in NRC, 1979]

Rose, C.S., R.A. Jones, L.J. Jenkins Jr., and J. Siegel. 1970. The acute hyperbaric toxicity of carbon monoxide. Toxicol. Appl Pharmacol 17:752-760.

Sawyer, C.N., and P.L. McCarty. 1978. Chemistry for Environmental Engineering, 3rd edition. McGraw-Hill Book Company, New York, New York. 532 p.

Sasiadek M, H Järventaus, M Sorsa. 1991. Sister-chromatid exchanges induced by 1,3-butadiene and its epoxides in CHO cells. *Mutat Res*. 263; 47-50.

Schmidt, U. and Loeser, E. 1985. Species differences in the formation of butadiene monoxide from 1,3-butadiene. Arch. Toxicol. **57**, 222-225.

Schwarzenbach, R.P., Gschwend, P.M., and Imboden, D.M., eds. 2003. Chapter 16: Indirect Photolysis: Reactions with Photooxidants in Natural Waters and in the Atmosphere. In: Environmental Organic Chemistry, 2nd Edition. John Wiley and Sons, Inc.

Sheraton D.F. and F.E. Murray. 1981. Can. J. Chem. 59: 2750-4. [Cited in: NLM (U.S. National Library of Medicine). 2005. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

Shimizu H. et al 1985 The results of microbial mutation test for forty-three industrial chemicals, Jap J Ind Health 27, 400-419.

Shugaev, BB (1969) Concentraions of hydrocarbons in tissues as a measure of toxicity. Arch. Environ. Health 18: 878-882.

Singh J and LH Scott. 1984. Threshold for carbon monoxide induced fetotoxicity. Teratology 30: 253-257.

Singh J. 1986. Early Behavioral Alterations in Mice Follwing Prenatal Carbon Monoxide Exposure. NeuroToxicology 7: 475-482.

Slikker, Jr, W, ME Andersen, MS Bogdanffy, *et al.* 2004. Dose-dependent transitions in mechanisms of toxicity: Case studies. *Tox Appl Pharm* 201: 226-94.

Smith, L.L., Jr. and D.M. Oseid. 1975. Chronic Effects of Low Levels of Hydrogen Sulfide on Freshwater Fish. Prog. Water Technol. 7(3/4):599-605.

Smith, L.L.J., D.M. Oseid, and L.E. Olson. 1976. Acute and Chronic Toxicity of Hydrogen Sulfide to the Fathead Minnow, Pimephales promelas. Environ. Sci. Technol. 10(6):565-568.

Speight, J. G. 2007. The Chemistry and Technology of Petroleum. Fourth Edition. CRC Press. Boca Raton, FL.

Stephens, S., C. De Sha, and R. Fuerst. 1971. Phenotypic and Genetic Effects in Neurospora crassa Produced by Selected Gases and Gases Mixed with Oxygen. Dev. Ind. Microbiol. 12:346-353.

Stolpe J, and Sedlag R. 1976. Die Einzel- und Komplexwirkung von Ammoniak und Schwefelwasserstoff in der Luft auf kleine Versuchstiere (Ratten) bei unterschiedlichen Umweltbedingungen. Ach. Exper. Vet. Med. 30: 533-539.

Swenberg, JA, G Boysen, N Georgieva, *et al.* 2007. Future directions in butadiene risk assessment and the role of cross-species internal dosimetry. *Chem Biol Inter* 166: 78-83.

Tansy MF, Kendall, FM, Fantasia, J, Landin, WE and R Oberly. 1981. Acute and subchronic toxicity studies of rats exposed to vapors of methyl mercaptan and other reduced-sulfur compounds. J Toxicol Environ Health, 8, 71-88.

TCEQ (Texas Commission on Environmental Quality). 2008. 1,3-Butadiene CAS Registry Number: 106-99-0. Available at http://www.tceq.state.tx.us/implementation/tox/dsd/final.html.

Thompson, PW. 1992. Butene-2 [2-butene]: Reverse mutation assay "Ames test" using *Salmonella typhimurium*. Proj. #44/812. SafePharm Laboratories, UK, Derby UK.

USEPA (United States Environmental Protection Agency). 1982. EPA Report, Air Quality Criteria for Carbon Monoxide, EPA 600/P-99/001F, June 2000U.S. FDA. 21 CFR Parts 182 and 184.

USEPA. 1984. Validation of chemical and biological techniques for evaluation of vapors in ambient air/mutagenicity testing of twelve (12) vapor-phase compounds. Research Triangle Park, NC: U.S. Environmental Protection Agency, Health Effects Research Laboratory. EPA600184005. PB84164219.U.S. Environmental Protection Agency. 1994a. Methods for Derivation of Reference Concentrations and Application of Inhalation Dosimetry. EPA/600/8-90/066F.

U.S. Environmental Protection Agency 1994b. Fuels and Fuels Additives Registration Regulations; Final Rule pursuant to the Clean Air Act 211(b), 211(e). 40 CFR Part 79, FR59, No. 122: 33042-33142 (27 June 1994). Washington, DC: EPA. 1994

USEPA. 1986a. Health and Environmental Effects Profile for Hydrogen Sulfide. Report No. ECAO-CIN-026A. [Cited in: NLM (U.S. National Library of Medicine). 2005. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

USEPA (United States Environmental Protection Agency). 1986b. Quality Criteria for Water: 1986. EPA 440/5-86-001, U.S. EPA, Office of Water, Washington, DC.US

U.S. Environmental Protection Agency. 1991. Alpha 2 microglobulin: association with chemically induced renal toxicity and neoplasia in the male rat. In Risk Assessment Forum. US Government Printing Office, Washington, DC: EPA: 85.

US EPA (U.S. Environmental Protection Agency). 1996. Series 870- Health Effects Test Guidelines, OPPTS Number 870.3550: Reproduction/Developmental Toxicity Screening Test.

U.S. Environmental Protection Agency. 1998. Fuels and Fuels Additives Registration Regulations; Final Revised 211(b) Tier 2 Testing Requirements. Correspondence to Director of Health and Environmental Sciences Dept., American Petroleum Institute. November 2, 1998.

USEPA. 1999. Determining the Adequacy of Existing Data. OPPT, EPA.

USEPA (U.S. Environmental Protection Agency). 2000a. EPI SuiteTM, the Estimation Programs Interface (EPI) SuiteTM. U.S. Environmental Protection Agency, Washington, DC.

USEPA. 2000b. EPA Report, Carbon Dioxide as a Fire Suppressant: Examining the Risks; EPA430-R-00-002.

USEPA. 2002a. Health Assessment of 1,3-Butadiene. EPA/600/P-98/001F. National Center for Environmental Assessment, Office of Research and Development, Washington D.C.U.S. Environmental Protection Agency. 2002b. A Review of the Reference Dose and Reference Concentration Processes. Report EPA/630/P-02/002F, Risk Assessment Forum, U.S. EPA, Washington, DC.

USEPA (U.S. Environmental Protection Agency). 2007a. ECOTOX User Guide: ECOTOXicology Database System. Version 4.0. Available: http:/www.epa.gov/ecotox/

U.S. Environmental Protection Agency. 2007b. Development of Chemical Categories in the HPV Challenge Program. www URL: http://www.epa.gov/HPV/pubs/general/categuid.htm (updated November 28, 2007)

US NLM (U.S. National Library of Medicine). 2007. Integrated Risk Information System (IRIS). www URL: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?IRIS

Venable C.S., and T. Fuwa. 1922. Ind Eng Chem 14: 139-42. [cited in NLM (U.S. National Library of Medicine). 2008. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

Vestal, J.R. 1984. The Metabolism of Gaseous Hydrocarbons by Microorganisms. In, Petroleum Microbiology, R. M. Atlas, ed. , MacMillan Publishing Co., New York, NY.

Visscher, P.T., and B.F. Taylor. 1993. Aerobic and Anaerobic Degradation of a Range of Alkyl Sulfides by a Denitrifying Marine Baceterium. App. Environ. Microbiol. 59(12):4083-4089.

Waalkens-Brendsen, D.H. and Arts, J.H.E. 1992. Combined short term inhalation and reproductive/developmental toxicity screening test with Butene-2 in rats. Proj.#B91-8336 (Study #1410) [2-butene]. As summarized in Low 1,3-Butadiene C4 Category, ACC Olefins panel, 2004.

Wakita, K., et al. 1986. Chem. Pharm. Bull. 34:4463-81. [Cited in: NLM (U.S. National Library of Medicine). 2006. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

Ward, CO, RA Kuna, NK Snyder, RD Alsaker, WB Coate, PH Craig (1985) Subchronic inhalation toxicity of benzene in rats and mice. Americ. Journ. of Industrial Medicine 7: 457-473.

Weast, R.C. (ed.). 1984 – 1985. Handbook of Chemistry and Physics. 65th ed. CRC Press, Inc. Boca Raton, FL., p. D-219. [Cited in: NLM (U.S. National Library of Medicine). 2008. Hazardous Substance Data Bank. Available through the TOXNET Toxicology Data Network, http://toxnet.nlm.nih.gov]

WHO (World Health Organization). 1979. Environmental Health Criteria No. 13: Carbon Monoxide. World Health Organization, Geneva, Switzerland. Accessed through http://www.inchem.org/ documents/ehc/ehc/ehc013.htm#SectionNumber:4.1.

WIL Research Laboratories. 2003. An inhalation reproduction/developmental toxicity screening study of 1,3-butadiene in rats (unpublished report). (WIL-186024). WIL Research Laboratories, Inc., Ashland, OH, USA.

World Health Organization (WHO). 1986. Ammonia – Environmental Health Criteria 54. Geneva: International Programme on Chemical Safety.

Wright, NP. 1992. Butene-2 [2-butene]: Metaphase analysis in rat lymphocytes *in vitro*. Proj. #44/813. SafePharm Laboratories, UK, Derby UK.

12 LIST OF APPREVIATIONS AND ACRONYMS[17]

AOP – atmospheric oxidation potential
API – American Petroleum Institute
atm-m^3/mole –atmosphere cubic meter per mole
BGVC – basline gasoline vapor condensate
CAS RN/CAS #/CAS No. - Chemical Abstract Service Registry Number
^oC – degrees Celsius
cm^3 – cubic centimeter
CO – carbon monoxide
CO_2 – carbon dioxide
CPK – cratinine phosphokinase
CONCAWE – Conservation of Clean Air and Water in Europe
d - day
DEB – 1,2,3,4-diepoxybutane
DMSO – Dimethyl sulfoxide
EC_{50} – concentration causing a specific response to 50% of the test population
ECB – European Chemicals Bureau
ECG - electrocardiogram
EB – 1,2-epoxy-3-butene
EBD – 1,2-dihydroxy-3,4-epoxybutane
EL_{50} – effective loading rate lethal to 50% of the test population
E_bL_{50} – effective loading rate that causes 50% reduction in algal cell biomass
E_rL_{50} – effective loading rate that causes 50% reduction in algal growth rate
EPA/USEPA – United States Environmental Protection Agency
FOB – functional observational battery
g/cm^3 – grams per cubic centimeter
g/kg – grams per kiligram
g/m^3 – grams per cubic meter
GOT – gutamic oxalacetic transaminase
H_2 – hydrogen
HCs - hydrocarbons
H_2S – hydrogen sulfide
HLS – Huntingdon Life Sciences
hPa - hectopascal
HPV – High Production Volume
hr - hour
IDLH – Immediately Dangerous to Life and Health
^oK – degrees Kelvin
L - liter
LC_{50} – lethal concentration for 50% of the test population
LD_{50}– lethal dose level for 50% of the test population
LDH – lactic dehydrogenase
LL_{50} – lethal loading rate for 50% of the test population
Loading Rate – total amount of test substance added to dilution water to prepare water accommodated fractions (WAFs) for ecotoxicity testing
LOAEL – lowest observable adverse effect level
log Kow – partitian coefficient
m^3 – cubic meter
MACT – maximum achievable control technology
mg/kg – milligrams per kilogram
mg/L – milligrams per liter
mg/m^3 – milligrams per cubic meter

[17] This is a generic list of abbreviations and acronyms; all terms may not appear within this particular document

mL - milliliter
mm - millimeter
N_2 - nitrogen
NH_3 - ammonia
nm - nanometer
NOAEL – no observable adverse effect level
NOEC – no observable effect concentration
NOELR – no observable effect loading rate
OECD – Organization for Economic Cooperation and Development
OPPTS – US EPA Office of Prevention, Pesticides and Toxic Substances
OH^- - hydroxyl radical
PCEs – polychromatic erythrocytes
PII – primary irritation score in skin irritation studies
pO_2 – partial pressure of oxygen
ppm – part per million
RBC – red blood cell
SCE – sister chromatid exchange
SIDS – Screening Information Data Set
SO_2 – sulfur dioxide
TSCA – Toxic Substances Control Act
US EPA – United States Environmental Protection Agency
UV - ultraviolet
WAF – water accommodated fraction
Wt/v% - weight per volume percent μg - microgram
μg/L – microgram/liter
μM - micromole
> greater than
< less than
= equal to

13. GLOSSARY[18]

NOTE: *The following terms are used in this document. To the extent possible definitions were taken from relevant authoritative sources such as US EPA, OECD, ASTM and IUPAC.*

Alpha 2-microglobulin mediated nephropathy: also identified as light hydrocarbon-induced nephropathy (LHN) is a species and sex-specific syndrome induced in male rats resulting from repeated exposure to volatile petroleum naphthas in the gasoline blending stream range. The syndrome is characterized by excessive formation of hyaline droplets comprised of the unique sex-hormone dependent alpha 2-microglobulin, in the epithelium of the proximal convoluted leading to degenerative changes in these tubules in the renal cortex and tubular dilatation and necrosis at the corticomedullary junction. Evaluation of nephrotoxicity of volatile hydrocarbons in male rats and comparison of effects in female rats and both sexes of other species (Alden et al., 1984) has confirmed the uniqueness of this syndrome in male rats and has resulted in the US EPA determination that alpha 2-microglobulin mediated nephrotoxicity is not relevant to health effects in humans. (US EPA, 1991).

Bioavailability: The state of being capable of being absorbed and available to interact with the metabolic processes of an organism. Typically a function of chemical properties, physical state of the material to which an organism is exposed, and the ability of the individual organism to physiologically take up the chemical. Also, the term used for the fraction of the total chemical in the environmental that is available for uptake by organisms. **(AIHA 2000)**

Category Member: The individual chemical or substance entities that constitute a chemical category.

Category: A chemical category, for the purposes of the HPV Challenge Program, is a group of chemicals whose physicochemical and toxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity. These structural similarities may create a predictable pattern in any or all of the following parameters: physicochemical properties, environmental fate and environmental effects, and/or human health effects. **(US EPA 2007b)**

Dose: The amount of a substance available for interactions with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism. The **potential dose** is the amount ingested, inhaled, or applied to the skin. The **applied dose** is the amount presented to an absorption barrier and available for absorption (although not necessarily having yet crossed the outer boundary of the organism). The **absorbed dose** is the amount crossing a specific absorption barrier (e.g., the exchange boundaries of the skin, lung, and digestive tract) through uptake processes. **Internal dose** is a more general term denoting the amount absorbed without respect to specific absorption barriers or exchange boundaries. The amount of the chemical available for interaction by a particular organ or cell is termed the delivered or **biologically effective dose** for that organ or cell **(US EPA 2002b).**

Dose-Response Relationship: The relationship between a quantified exposure (dose) and the proportion of subjects demonstrating specific biological changes in incidence or in degree of change (response) **(US EPA 2002b).**

Ecological Effects – all endpoints (OECD definitions)

> **Fish, Acute Toxicity Test:** In a four-day exposure, acute toxicity is defined by the LC_{50}, the concentration of test substance in water which kills 50% of the test population of fish. Test methodology is described in OECD Guideline 203, in OECD Guidelines for the Testing of Chemicals.
>
> ***Daphnia* sp., Acute Immobilization Test:** In a one or two-day exposure, acute toxicity is defined by the EC_{50}, the concentration of test substance in water which causes immobilization to 50% of the test population of invertebrates. Test methodology is described in OECD Guideline 202, Part 1, in OECD Guidelines for the Testing of Chemicals.

[18] This is a generic glossary; all terms may not appear within this particular document

Alga, Growth Inhibition Test: In a three-day exposure, growth inhibition is defined by the EC_{50}, the concentration of test substance in growth medium which results in a 50% reduction in either alga cell growth or growth rate relative to a control group. Test methodology is described in OECD Guideline 201, in OECD Guidelines for the Testing of Chemicals.

Endpoint: In the context of the EPA High Production Volume Challenge Program, an endpoint is a physical-chemical, environmental fate, ecotoxicity, and human health attribute measurable by following an approved test methodology (e.g., OECD Guidelines for Testing of Chemicals). Melting point, biodegradation, fish acute toxicity, and genetic toxicity are examples of endpoints that are measured by an approved test method. **(US EPA 1999)**

Environmental Fate Effects – all endpoints (OECD definitions)

Photodegradation: The photochemical transformation of a molecule into lower molecular weight fragments, usually in an oxidation process. This process may be measured by Draft OECD Guideline, "*Phototransformation of Chemicals in Water – Direct and Indirect Photolysis*". This process also may be estimated using a variety of computer models.

Stability in Water: This environmental fate endpoint is achieved by measuring the hydrolysis of the test substance. Hydrolysis is defined as a reaction of a chemical RX with water, with the net exchange of the group X with OH at the reaction center. Test methodology for hydrolysis is described in OECD Guideline 111, in OECD Guidelines for the Testing of Chemicals.

Transport Between Environmental Compartments: This endpoint describes the distribution of a chemical between environmental compartments using fugacity-based computer models. The results of the model algorithms provide an estimate of the amount of the chemical within a specific compartment. The environmental compartments included in many models are air, water, soil, sediment, suspended sediment, and aquatic biota.

Biodegradation: Breakdown of a substance catalyzed by enzymes *in vitro* or *in vivo*. As an endpoint in EPA's HPV program, biodegradation is measured by one of six methodologies described in OECD Guidelines 301A-F, in OECD Guidelines for the Testing of Chemicals.

Exposure: Contact made between a chemical, physical, or biological agent and the outer boundary of an organism. Exposure is quantified as the amount of an agent available at the exchange boundaries of the organism (e.g., skin, lungs, gut). **(US EPA 2002b).**

Feedstock: A refinery product that is used as the raw material for another process; the term is also generally applied to raw materials used in other industrial processes. **(Speight, 2007).**

Female Mating Index: Number of females with confirmed mating (sperm and/or vaginal plug)/number of females placed with males. (**US EPA 1996).**

Formulated Gasoline: Unleaded automotive fuel formulated by blending paraffinic, olefinic, naphthenic and aromatic petroleum naphtha that does not contain oxygenates (e.g. methyl tertiary butyl ether, ethanol, etc.)**..**

Hazard Assessment: The process of determining whether exposure to an agent can cause an increase in the incidence of a particular adverse health effect (e.g., cancer, birth defect) and whether the adverse health effect is likely to occur in humans **(US EPA 2002b)**.

Hazard Characterization: A description of the potential adverse health effects attributable to a specific environmental agent, the mechanisms by which agents exert their toxic effects, and the associated dose, route, duration, and timing of exposure **(US EPA 2002b).**

Hazard: A potential source of harm **(US EPA 2002b**).

Health Effects – all endpoints (OECD definitions, unless otherwise specified)

Acute Toxicity: The adverse effects occurring within a short time-frame of administration of a single dose of a substance, multiple doses given within 24 hours, or uninterrupted exposure over a period of 24 hours or less. Exposure may be via oral, dermal or inhalation routes as described in OECD Guidelines 401, 402, 403, and 420 in OECD Guidelines for the Testing of Chemicals.

Developmental Toxicity: Adverse effects on the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally until the time of sexual maturation. The major manifestations of developmental toxicity include death of the developing organism, structural abnormality, altered growth, and functional deficiency. **(US NLM 2007)**

Genetic Toxicity *in vivo* (Chromosomal Aberrations): The assessment of the potential of a chemical to exert adverse effects through interaction with the genetic material of cells in the whole animal. Genotoxicity may be studies in the whole animal using methods described in OECD Guideline 475, in OECD Guidelines for the Testing of Chemicals.

Genetic Toxicity *in vitro* (Gene Mutations): The assessment of the potential of a chemical to exert adverse effects through interaction with the genetic material of cells in cultured mammalian cells. Genotoxicity may be studies in cultured cells using methods described in OECD Guideline 476, in OECD Guidelines for the Testing of Chemicals.

Repeated Dose Toxicity: The adverse effects occurring due to repeated doses that may not produce immediate toxic effects, but due to accumulation of the chemical in tissues or other mechanisms, produces delayed effects. Repeated dose toxicity may be studied following methods described in OECD Guidelines 407, 410, or 412 in OECD Guidelines for the Testing of Chemicals.

Reproductive Toxicity: The occurrence of biologically adverse effects on the reproductive systems of females or males that may result from exposure to environmental agents. The toxicity may be expressed as alterations to the female or male reproductive organs, the related endocrine system, or pregnancy outcomes. The manifestation of such toxicity may include, but not be limited to, adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behavior, fertility, gestation, parturition, lactation, developmental toxicity, premature reproductive senescence, or modifications in other functions that are dependent on the integrity of the reproductive systems. **(US EPA 1996)**

Light hydrocarbon induced nephrotoxicity (LHN): also identified as alpha 2-microglobulin mediated nephropathy. See definition above.

Lowest-Observed-Adverse-Effect Level (LOAEL): The lowest exposure level at which there are statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group **(US EPA 2002b).**

No-Observed-Adverse-Effect Level (NOAEL): The highest exposure level at which there are no biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group; some effects may be produced at this level, but they are not considered adverse or precursors to adverse effects **(US EPA 2002b)**.

Petroleum (crude oil): A naturally occurring mixture of gaseous, liquid, and solid hydrocarbon compounds usually found trapped deep underground beneath impermeable cap rock and above a lower dome of sedimentary rock such as shale; most petroleum reservoirs occur in sedimentary rocks of marine, deltaic, or estuarine origin **(Speight 2007)**.

Portal of Entry Effect: A local effect produced at the tissue or organ of first contact between the biological system and the toxicant **(US EPA 1994a)**.

Read Across: Read-across can be regarded as using data available for some members of a category to estimate values (qualitatively or quantitatively) for category members for which no such data exist. **(OECD 2007)**

Systemic Effects or Systemic Toxicity: Toxic effects as a result of absorption and distribution of a toxicant to a site distant from its entry point **(US EPA 2002b)**.

Target Organ: The biological organ(s) most adversely affected by exposure to a chemical or physical agent **(US EPA 2002b).**

APPENDIX 1

Refinery Gases Category Members by CASRN [1,2]

CAS number

000071-43-2 Supplemental Chemical
Benzene
No definition
(EU Category: none)

000074-93-1 Supplemental Chemical
Methanethiol
No definition
(EU Category: none; overlap with Mercaptans/Thiols Council[19] [MTC])

000075-08-1 Supplemental Chemical
Ethanethiol
No definition
(EU Category: none)

000075-28-5 Supplemental Chemical (for C1 – C4 HC fraction)
I*sobutane*
No definition
(EU Category: none)

000106-98-9 Supplemental Chemical (for C1 – C4 HC fraction)
1-Butene
No definition
(EU Category: none; overlap with American Chemicstry Council[20] [ACC])

000106-99-0 Supplemental Chemical
1,3-Butadiene
No definition
(EU Category: none; overlap with ACC)

000107-01-7 Supplemental Chemical (for C1 – C4 HC fraction)
2-Butene
No definition
(EU Category: none; overlap with ACC)

000124-38-9 (Supplemental Chemical)
Carbon dioxide
No definition
(EU Category: none)

000630-08-0 (Supplemental Chemical)
Carbon monoxide
No definition
(EU Category: none)

001333-74-0 (Supplemental Chemical)
Hydrogen
No definition
(EU Category: none)

005188-07-8 (Supplemental Chemical - for hydrogen sulfide and mercaptans, only)
Methanethiol, sodium salt
No definition
(EU Category: none; overlap with MTC)

[19] The CASRN is also a member of the Mercaptans/Thiols Council's *Methyl Mercaptan and Methyl Mercaptide HPV Category*

[20] The CASRN is also a member of one the American Chemistry Council's Olefins Panel HPV categories: *Crude Butadiene C4 Butadiene Category; Low 1,3-Butadiene C4 Category; or Pyrolysis C3+ and Pyrolysis C4+ Category*

007664-41-7 (Supplemental Chemical)
Ammonia
No definition
[EU Category: none]

007727-37-9 (Supplemental Chemical)
Nitrogen
No definition
[EU Category: none]

007783-06-4 (Supplemental Chemical)
Hydrogen sulfide
No definition
[EU Category: none]

008006-20-0
Fuel gases. Low and medium BTU
A complex combination obtained by burning coal or coke with a restricted air or oxygen supply or by blowing air or oxygen and steam through incandescent coke. The combustibles consist primarily of carbon monoxide, carbon dioxide and hydrogen.

068308-27-0
Fuel gases, refinery
A complex combination of light gases consisting of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C5.
[EU Category: Petroleum Gases (Petroleum Gas)]

068476-26-6
Fuel gases
A combination of light gases. It consists predominantly of hydrogen and/or low molecular weight hydrocarbons.
[EU Category: Petroleum Gases (Petroleum Gas)]

068476-27-7
Fuel gases, amine system residues
The complex residuum from the amine system for removal of hydrogen sulfide. It consists primarily of hydrogen, methane and ethane with various small amounts of nitrogen, carbon dioxide and hydrocarbons having carbon numbers predominantly in the range of C3 through C5.
[EU Category: Petroleum Gases (Petroleum Gas)]

068476-28-8
Fuel gases, C6-8 catalytic reformer
A complex combination of gases obtained from a catalytic reforming process using C6-8 hydrocarbon feed. It consists primarily of hydrogen and methane with various small amounts of nitrogen, carbon monoxide, carbon dioxide and hydrocarbons having carbon numbers predominantly in the range of C2 through C6.
[EU Category: Petroleum Gases (Petroleum Gas)]

068476-29-9
Fuel gases, crude oil distillates
A complex combination of light gases produced by distillation of crude oil and by catalytic reforming of naphtha. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C4 and boiling in the range of approximately -217°C to -12°C (-423°F to 10°F).
[EU Category: Other Petroleum Gases (Refinery Gas)]

068477-65-6
Gases (petroleum), amine system feed
The feed to the amine system for removal of hydrogen sulfide. It consists of hydrogen, carbon monoxide, carbon dioxide, hydrogen sulfide and aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C5.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068477-66-7

Gases (petroleum), benzene unit hydrodesulfurizer off

Off gases produced by the benzene unit. It consists primarily of hydrogen. Carbon monoxide and hydrocarbons having carbon numbers predominantly in the range of C1 through C6, including benzene, may also be present.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068477-67-8

Gases (petroleum), benzene unit recycle, hydrogen-rich

A complex combination of hydrocarbons obtained by recycling the gases of the benzene unit. It consists primarily of hydrogen with various small amounts of carbon monoxide and hydrocarbons having carbon numbers in the range of C1 through C6.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068477-68-9

Gases (petroleum), blend oil, hydrogen-nitrogen-rich

A complex combination of hydrocarbons obtained by distillation of a blend oil. It consists primarily of hydrogen and nitrogen with various small amounts of carbon monoxide, carbon dioxide, and aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C5.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068477-77-0

Gases (petroleum), catalytic reformed naphtha stripper overheads

A complex combination of hydrocarbons obtained from the stabilization of catalytic reformed naphtha. It consists of hydrogen and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C4.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068477-80-5

Gases (petroleum), C6-8 catalytic reformer recycle

A complex combination of hydrocarbons produced by distillation of products from catalytic reforming of C6-C8 feed and recycled to conserve hydrogen. It consists primarily of hydrogen. It may also contain various small amounts of carbon monoxide, carbon dioxide, nitrogen, and hydrocarbons having carbon numbers predominantly in the range of C1 through C6.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068477-81-6

Gases (petroleum), C6-8 catalytic reformer

A complex combination of hydrocarbons produced by distillation of products from catalytic reforming of C6-C8 feed. It consists of hydrocarbons having carbon numbers in the range of C1 through C5 and hydrogen.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068477-82-7

Gases (petroleum), C6-8 catalytic reformer recycle, hydrogen-rich

No definition

[EU Category: Other Petroleum Gases (Refinery Gas)]

068477-92-9

Gases (petroleum), dry sour, gas-concn.-unit-off

The complex combination of dry gases from a gas concentration unit. It consists of hydrogen, hydrogen sulfide and hydrocarbons having carbon numbers predominantly in the range of C1 through C3.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068477-95-2

Gases (petroleum), Girbatol unit feed

A complex combination of hydrocarbons that is used as the feed into the Girbatol unit to remove hydrogen sulfide. It consists of aliphatic hydrocarbons having carbon numbers

predominantly in the range of C2 through C4.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068477-97-4

Gases (petroleum), hydrogen-rich
A complex combination separated as a gas from hydrocarbon gases by chilling. It consists primarily of hydrogen with various small amounts of carbon monoxide, nitrogen, methane, and C2 hydrocarbons.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068477-98-5

Gases (petroleum), hydrotreater blend oil recycle, hydrogen-nitrogen-rich
A complex combination obtained from recycled hydrotreated blend oil. It consists primarily of hydrogen and nitrogen with various small amounts of carbon monoxide, carbon dioxide and hydrocarbons having carbon numbers predominantly in the range of C1 through C5.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068478-00-2

Gases (petroleum), recycle, hydrogen-rich
A complex combination obtained from recycled reactor gases. It consists primarily of hydrogen with various small amounts of carbon monoxide, carbon dioxide, nitrogen, hydrogen sulfide, and saturated aliphatic hydrocarbons having carbon numbers in the range of C1 through C5.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068478-01-3

Gases (petroleum), reformer make-up, hydrogen-rich
A complex combination obtained from the reformers. It consists primarily of hydrogen with various small amounts of carbon monoxide and aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C5.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068478-02-4

Gases (petroleum), reforming hydrotreater
A complex combination obtained from the reforming hydrotreating process. It consists primarily of hydrogen, methane, and ethane with various small amounts of hydrogen sulfide and aliphatic hydrocarbons having carbon numbers predominantly in the range of C3 through C5.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068478-03-5

Gases (petroleum), reforming hydrotreater, hydrogen-methane-rich
A complex combination obtained from the reforming hydrotreating process. It consists primarily of hydrogen and methane with various small amounts of carbon monoxide, carbon dioxide, nitrogen and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of C2 through C5.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068478-04-6

Gases (petroleum), reforming hydrotreater make-up, hydrogen-rich
A complex combination obtained from the reforming hydrotreating process. It consists primarily of hydrogen with various small amounts of carbon monoxide and aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C5.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068478-05-7

Gases (petroleum), thermal cracking distn.
A complex combination produced by distillation of products from a thermal cracking process. It consists of hydrogen, hydrogen sulfide, carbon monoxide, carbon dioxide and hydrocarbons having carbon numbers predominantly in the range of C1 through C6.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068478-25-1

Tail gas (petroleum), catalytic cracker refractionation absorber

A complex combination of hydrocarbons obtained from refractionation of products from a catalytic cracking process. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C3.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068478-27-3

Tail gas (petroleum), catalytic reformed naphtha separator

A complex combination of hydrocarbons obtained from the catalytic reforming of straight run naphtha. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C6.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068478-28-4

Tail gas (petroleum), catalytic reformed naphtha stabilizer

A complex combination of hydrocarbons obtained from the stabilization of catalytic reformed naphtha. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C6.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068478-29-5

Tail gas (petroleum), cracked distillate hydrotreater separator

A complex combination of hydrocarbons obtained by treating cracked distillates with hydrogen in the presence of a catalyst. It consists of hydrogen and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C5.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068478-30-8

Tail gas (petroleum), hydrodesulfurized straight-run naphtha separator

A complex combination of hydrocarbons obtained from hydrodesulfurization of straight-run naphtha. It consists of hydrogen and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C6.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068513-11-1

Fuel gases, hydrotreater fractionation, scrubbed

A complex combination produced by the fractionation and scrubbing of products from various hydrotreating units. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C4.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068513-13-3

Fuel gases, thermal cracked catalytic cracking residue

A complex combination obtained by the thermal cracking of a catalytically cracked residuum. It consists of hydrogen and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C4.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068513-14-4

Gases (petroleum), catalytic reformed straight-run naphtha stabilizer overheads

A complex combination of hydrocarbons obtained from the catalytic reforming of straight-run naphtha followed by fractionation of the total effluent. It consists of hydrogen, methane, ethane and propane.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068513-16-6

Gases (petroleum), hydrocracking depropanizer off, hydrocarbon-rich

A complex combination of hydrocarbon produced by the distillation of products from a hydrocracking process. It consists predominantly of hydrocarbons having carbon numbers predominantly in the range of C1 through C4. It may also contain small amounts of hydrogen and hydrogen sulfide.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068513-18-8

Gases (petroleum), reformer effluent high-pressure flash drum off

A complex combination produced by the high-pressure flashing of the effluent from the reforming reactor. It consists primarily of hydrogen with various small amounts of methane, ethane, and propane.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068513-19-9

Gases (petroleum), reformer effluent low-pressure flash drum off

A complex combination produced by low-pressure flashing of the effluent from the reforming reactor. It consists primarily of hydrogen with various small amounts of methane, ethane, and propane.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068513-68-8

Residues (petroleum), deethanizer tower

A complex residuum from the distillation of a gas stream containing hydrogen, carbon monoxide, carbon dioxide and hydrocarbons having carbon numbers in the range of C1 through C6 or from the cracking of ethane and propane. It consists of hydrocarbons having carbon numbers in the range of C2 through C6. It may contain small amounts of benzene.

[EU Category: Other Petroleum Gases (Refinery Gas); overlaps with ACC]

068527-13-9

Gases (petroleum), acid, ethanolamine scrubber

A complex mixture separated from refinery gas by scrubbing with ethanolamine. It consists primarily of hydrogen sulfide and carbon dioxide. It may also contain various small amounts of hydrogen, carbon monoxide and nitrogen.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068527-14-0 (not HPV listed)

Gases (petroleum), methane-rich off ..C1

A complex combination separated by distillation of a gas stream containing hydrogen, carbon monoxide, carbon dioxide and hydrocarbons having carbon numbers in the range of C1 through C6 or obtained by the cracking of ethane and propane. It consists primarily of methane with various small amounts of hydrogen and nitrogen.

[EU Category: Petroleum Gases (Petroleum Gas)]

068527-15-1

Gases (petroleum), oil refinery gas distn. off

A complex combination separated by distillation of a gas containing hydrogen, carbon monoxide, carbon dioxide and hydrocarbons having carbon numbers in the range of C1 through C6 or obtained by cracking ethane and propane. It consists of hydrocarbons having carbon numbers predominantly in the range of C1 through C2, hydrogen, nitrogen, and carbon monoxide.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068602-82-4

Gases (petroleum), benzene unit hydrotreater dependanizer overheads

A complex combination produced by treating the feed from the benzene unit with hydrogen in the presence of a catalyst followed by dependanizing. It consists primarily of hydrogen, ethane and propane with various small amounts of nitrogen, carbon monoxide, carbon dioxide and hydrocarbons having carbon numbers predominantly in the range of C1 through C6. It may contain trace amounts of benzene.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068602-84-6

Gases (petroleum), secondary absorber off, fluidized catalytic cracker overheads fractionator

A complex combination produced by the fractionation of the overhead products from the

catalytic cracking process in the fluidized catalytic cracker. It consists of hydrogen, nitrogen, and hydrocarbons having carbon numbers predominantly in the range of C1 through C3.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068607-11-4

Petroleum products, refinery gases
A complex combination which consists primarily of hydrogen with various small amounts of methane, ethane, and propane.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068783-05-1

Gases (petroleum), ammonia-hydrogen sulfide, water-satd.
A water-saturated gas produced by the treatment of waste process water through steam stripping. It consists of up to 30% hydrogen sulfide and up to 60% ammonia.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068783-06-2

Gases (petroleum), hydrocracking low-pressure separator
A complex combination obtained by the liquid vapor separation of the hydrocracking process reactor effluent. It consists predominantly of hydrogen and saturated hydrocarbons having carbon numbers predominantly in the range of C1 through C3.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068783-07-3

Gases (petroleum), refinery blend
A complex combination obtained from various refinery processes. It consists of hydrogen, hydrogen sulfide and hydrocarbons having carbon numbers predominantly in the range of C1 through C5.
[EU Category: Petroleum Gases (Petroleum Gas)]

068783-62-0

Fuel gases, refinery, unsweetened
A complex combination obtained by the fractionation of naphtha and compressed hydrocarbon gas streams from various refinery processes. It consists predominantly of hydrocarbons having carbon numbers predominantly in the range of C1 through C5 and boiling in the range of -73°C to 65°C (-100°F to 150°F).
[EU Category: Other Petroleum Gases (Refinery Gas)]

068814-47-1

Waste gases, refinery vent
A complex combination obtained from various refinery processes. It consists of hydrocarbons having carbon numbers predominantly in the range of C1 through C5 and hydrogen sulfide.
(EU Category: Refinery Gases, Category 2)

068814-67-5

Gases (petroleum), refinery
A complex combination obtained from various petroleum refining operations. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C3.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068814-90-4

Gases (petroleum), platformer products separator off
A complex combination obtained from the chemical reforming of naphthenes to aromatics. It consists mainly of hydrogen and saturated hydrocarbons having carbon numbers predominantly in the range of C2 through C4.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068911-58-0

Gases (petroleum), hydrotreated sour kerosine dependanizer stabilizer off
The complex combination obtained from the dependanizer stabilization of hydrotreated

kerosine. It consists primarily of hydrogen, methane, ethane, and propane with various small amounts of nitrogen, hydrogen sulfide, carbon monoxide and hydrocarbons having carbon numbers predominantly in the range of C4 through C5.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068911-59-1

Gases (petroleum), hydrotreated sour kerosine flash drum
A complex combination obtained from the flash drum of the unit treating sour kerosine with hydrogen in the presence of a catalyst. It consists primarily of hydrogen and methane with various small amounts of nitrogen, carbon monoxide, and hydrocarbons having carbon numbers predominantly in the range of C2 through C5.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068919-01-7

Gases (petroleum), distillate unifiner desulfurization stripper off
A complex combination stripped from the liquid product of the unifiner desulfurization process. It consists of hydrogen sulfide, methane, ethane, and propane.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068919-02-8

Gases (petroleum), fluidized catalytic cracker fractionation off
A complex combination produced by the fractionation of the overhead product of the fluidized catalytic cracking process. It consists of hydrogen, hydrogen sulfide, nitrogen, and hydrocarbons having carbon numbers predominantly in the range of C1 through C5.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068919-03-9

Gases (petroleum), fluidized catalytic cracker scrubbing secondary absorber off
A complex combination produced by scrubbing the overhead gas from the fluidized catalytic cracker. It consists of hydrogen, nitrogen, methane, ethane and propane.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068919-04-0

Gases (petroleum), heavy distillate hydrotreater desulfurization stripper off
A complex combination stripped from the liquid product of the heavy distillate hydrotreater desulfurization process. It consists of hydrogen, hydrogen sulfide, and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of Cl through C5.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068919-07-3

Gases (petroleum), platformer stabilizer off, light ends fractionation
A complex combination obtained by the fractionation of the light ends of the platinum reactors of the platformer unit. It consists of hydrogen, methane, ethane, and propane.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068919-08-4

Gases (petroleum), preflash tower off, crude distn.
A complex combination produced from the first tower used in the distillation of crude oil. It consists of nitrogen and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C5
[EU Category: Other Petroleum Gases (Refinery Gas)]

068919-12-0

Gases, (petroleum) unifiner stripper
A combination of hydrogen and methane obtained by fractionation of the products from the unifiner unit.
[EU Category: Other Petroleum Gases (Refinery Gas)]

068952-79-4

Tail gas (petroleum), catalytic hydrodesulfurized naphtha separator
A complex combination of hydrocarbons obtained from the hydrodesulfurization of naphtha. It consists of hydrogen, methane, ethane, and propane.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068952-80-7

Tail gas (petroleum), straight-run naphtha hydrodesulfurizer

A complex combination obtained from the hydrodesulfurization of straight-run naphtha. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C5.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068955-33-9

Gases (petroleum), sponge absorber off, fluidized catalytic cracker and gas oil desulfurizer overhead fractionation

A complex combination obtained by the fractionation of products from the fluidized catalytic cracker and gas oil desulfurizer. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C4.

[EU Category: Other Petroleum Gases (Refinery Gas)]

068989-88-8

Gases (petroleum), crude distn. and catalytic cracking

A complex combination produced by crude distillation and catalytic cracking processes. It consists of hydrogen, hydrogen sulfide, nitrogen, carbon monoxide and paraffinic and olefinic hydrocarbons having carbon numbers predominantly in the range of C1 through C6.

[EU Category: Other Petroleum Gases (Refinery Gas)]

Note 1

There are a total of 76 CAS numbers included in the Refinery Gases Category. Of these 76, 61 are listed on the HPV substances list. Fourteen are supplemental chemicals (nine inorganic chemicals plus five hydrocarbons) included to characterize the SIDS endpoints for the refinery gases. The Testing Group has included one additional CAS number (68527-14-0) that covers a substance similar to those on the HPV list, but is not a designated HPV substance; it is noted by a '(not HPV listed)' designation after the respective CAS number. The supplemental chemicals are noted by a (supplemental chemical) designation after their respective CAS numbers.

Note 2

The Petroleum HPV Testing Group has included in its listing of CAS numbers an indication of the corresponding category adopted by the European Union (EU) in their legislation (Official Journal of the European Communities, L84 Volume 36, 5 April 1993, *Council Regulation (EEC) No 793/93 of 23 March 1993 on the evaluation and control of risks of existing substances*). The EU category information is being included in this test plan to facilitate the international harmonization of classification and the coordination of efforts to summarize existing data and develop new hazard data that will be appropriate for hazard and risk characterization worldwide. In doing so, it will help avoid unnecessary duplication of testing.

APPENDIX 2

Refinery Gases Category Member Component Concentration Ranges by CASRN

Sources of Composition Data Concerning the Refinery Gases

The petroleum process streams designated as Refinery Gases are normally site-limited intermediates or waste materials, not products for commercial sale, and definitely not "finished" to meet formal specifications. These streams contain one or more inorganic compounds with variable concentrations and at least one component with high enough concentration to be toxic and/or cause oxygen depletion in a closed space.

The compositions provided in this table of Refinery Gases are based upon limited historical (1992 through 2002) data from several US petrochemical and petroleum company refineries in the Gulf Coast and Mid-continent areas. These facilities processed mostly heavy (high viscosity), sour (high sulfur content) crude oils of Venezuelan and Mexican origin. These compositions did not necessarily reflect the concentration ranges for streams with the same Chemical Abstract Service Registry Numbers (CASRN) for East and West Coast refineries or other refineries processing light viscosity or sweet crude oils. Current sample analyses may not be representative of the average concentration ranges displayed because regulatory control of sulfur- and nitrogen-containing compounds is much more stringently controlled by enhanced processing, especially at West Coast refineries. Although these compositional ranges for the inorganic constituents, benzene, and butadiene of these particular Refinery Gases are considered to err on the side of higher, rather than lower concentrations, they are considered to be plausible, and have been used to derive refinery gas toxicity values that have been corrected for concentration.

Gas chromatography and/or mass spectrophotometer analysis of these Refinery Gas streams is not done for routine (daily, weekly, or monthly) process control purposes. Test samples are collected only when specific questions arise. Examples of reasons for non-routine compositional testing include temporary on-site storage, off-site transfer (via pipeline), corrosion control, planned process modifications, Material Safety Data Sheet (MSDS) creation or update, and/or the addition or modification of environmental monitoring and control equipment.

Concentration ranges of specific gas components may vary drastically depending upon crude oil sources, operating conditions, seasonal process issues, and economic cycles. The inorganic constituents identified in these Refinery Gas streams include hydrogen, ammonia, hydrogen sulfide, methyl mercaptan, ethyl mercaptan, carbon monoxide, and carbon dioxide. If nitrogen is present at significant levels in the stream, it was also included because of its' oxygen replacement property. No effort was made to identify individual hydrocarbon compound ranges present in these streams. The complex hydrocarbon mixture component is identified only by its carbon number range for the total mixtures, C1 – C4 and C5 – C6. In several streams containing C4 through C6 hydrocarbons, the presence of a few potentially carcinogenic hydrocarbon components (butadiene and benzene at concentrations exceeding 0.1 wt.%) has been included, even though they are not identified in the Refinery Gas stream's CASRN definition.

The compositional ranges for the 62 refinery gases are presented below in two different organizational formats to make finding specific information easier for the reader. Appendix Table 2-1 presents the gases component concentrations by CASRN, Gas Name, and TSCA Definition. To more easily see what components are present in each refinery stream, and at what concentration ranges, the same data presented in Appendix Table 2.1 is presented in Appendix Table 2.2 by CASRN and Component Ranges, only.

Appendix Table 2-1. Component Concentration Ranges for Refinery Gases by CASRN, Gas Name, and TSCA Definition

CAS Number	Petroleum Refinery Gas Name	TSCA Definition	Refinery Gas Composition Ranges
8006-20-0	Fuel gases, producer gas	A complex combination obtained by burning coal or coke with a restricted air supply or by blowing air and steam through incandescent coke. It consists primarily of nitrogen, carbon dioxide, carbon monoxide and hydrogen.	Hydrogen = 20 to 30%; Nitrogen = 20 to 30%; Carbon monoxide = 20 to 30%; Carbon dioxide = 20 to 30%; C1-C4 HCs = 1 to 10%.
68308-27-0	Fuel gases, refinery	A complex combination of light gases consisting of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C5.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; Butadiene = 0.1 to 2%; C1-C4 HCs = 37 to 58.5%; C5-C6 HCs = 0.5 to 3%.
68476-26-6	Fuel gases	A combination of light gases. It consists predominantly of hydrogen and/or low molecular weight hydrocarbons.	Hydrogen = 40 to 88%; Nitrogen = 1 to 5%; Ammonia = 0.01 to 0.2%; Hydrogen sulfide = 0.01 to 0.5%; Carbon monoxide = 0.5 to 5%; Carbon dioxide = 0.1 to 3%; C1-C4 HCs = 10 to 58%.
68476-27-7	Fuel gases, amine system residues	The complex residuum from the amine system for removal of hydrogen sulfide. It consists primarily of hydrogen, methane and ethane with various small amounts of nitrogen, carbon dioxide and hydrocarbons having carbon numbers predominantly in the range of C3 through C5.	Hydrogen = 40 to 59%; Nitrogen = 0.5 to 5%; Carbon monoxide = 0.5 to 5%; Carbon dioxide = 0.1 to 3%; C1-C4 HCs = 37 to 49.5%; C5-C6 HCs = 0.5 to 3%.
68476-28-8	Fuel gases, C6-8 catalytic reformer	A complex combination of gases obtained from a catalytic reforming process using C6-8 hydrocarbon feed. It consists primarily of hydrogen and methane with various small amounts of nitrogen, carbon monoxide, carbon dioxide and hydrocarbons having carbon numbers predominantly in the range of C2 through C6.	Hydrogen = 35 to 45%; Nitrogen = 1 to 10%; Carbon monoxide = 0.5 to 10%; Carbon dioxide = 0.1 to 5%; C1-C4 HCs = 25 to 40%; C5-C6 HCs = 5 to 10%.
68476-29-9	Fuel gases, crude oil distillates	A complex combination of light gases produced by distillation of crude oil and by catalytic reforming of naphtha. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C4 and boiling in the range of approximately -217°C to -12°C (-423°F to 10°F).	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; Butadiene = 0.1 to 2%; C1-C4 HCs = 40 to 59%.

Appendix Table 2-1. Component Concentration Ranges for Refinery Gases by CASRN, Gas Name, and TSCA Definition

CAS Number	Petroleum Refinery Gas Name	TSCA Definition	Refinery Gas Composition Ranges
68477-65-6	Gases (petroleum), amine system feed	The feed to the amine system for removal of hydrogen sulfide. It consists of hydrogen, carbon monoxide, carbon dioxide, and hydrogen sulfide; and, aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C5 may also be present.	Hydrogen = 30 to 50%; Ammonia = 0.1 to 10%; Hydrogen sulfide = 10 to 25%; Carbon monoxide = 0.5 to 15%; Carbon dioxide = 0.1 to 10%; C1-C4 HCs = 0.9 to 9%; C5-C6 HCs = 0.1 to 1%.
68477-66-7	Gases (petroleum), benzene unit hydrodesulfurizer off	Off gases produced by the benzene unit. It consists primarily of hydrogen. Carbon monoxide and hydrocarbons having carbon numbers predominantly in the range of C1 through C6, including benzene, may also be present.	Hydrogen = 50 to 75%; Carbon monoxide = 0.5 to 20%; Carbon dioxide = 0.1 to 10%; Benzene = 0.1 to 2%; C1-C4 HCs = 0.3 to 13%; C5-C6 HCs = 0.7 to 7%.
68477-67-8	Gases (petroleum), benzene unit recycle, hydrogen-rich	A complex combination of hydrocarbons obtained by recycling the gases of the benzene unit. It consists primarily of hydrogen with various small amounts of carbon monoxide and hydrocarbons having carbon numbers in the range of C1 through C6.	Hydrogen = 60 to 80%; Carbon monoxide = 0.5 to 15%; Carbon dioxide = 0.1 to 5%; Benzene = 0.1 to 2%; C1-C4 HCs = 0.3 to 13%; C5-C6 HCs = 0.7 to 7%.
68477-68-9	Gases (petroleum), blend oil, hydrogen-nitrogen-rich	A complex combination of hydrocarbons obtained by distillation of a blend oil. It consists primarily of hydrogen and nitrogen with various small amounts of carbon monoxide, carbon dioxide, and aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C5.	Hydrogen = 30 to 50%; Nitrogen = 20 to 40%; Carbon monoxide = 0.5 to 20%; Carbon dioxide = 0.1 to 10%; C1-C4 HCs = 0.9 to 18%; C5-C6 HCs = 0.1 to 2%.
68477-77-0	Gases (petroleum), catalytic reformed naphtha stripper overheads	A complex combination of hydrocarbons obtained from the stabilization of catalytic reformed naphtha. It consists of hydrogen and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C4.	Hydrogen = 40 to 60%; C1-C4 HCs = 40 to 60%.
68477-80-5	Gases (petroleum), C6-8 catalytic reformer recycle	A complex combination of hydrocarbons produced by distillation of products from catalytic reforming of C6-C8 feed and recycled to conserve hydrogen. It consists primarily of hydrogen. It may also contain various small amounts of carbon monoxide, carbon dioxide, nitrogen, and hydrocarbons having carbon numbers predominantly in the range of C1 through C6.	Hydrogen = 40 to 60%; Nitrogen = 1 to 15%; Carbon monoxide = 0.5 to 15%; Carbon dioxide = 0.1 to 5%; Benzene = 0.1 to 2%; C1-C4 HCs = 1 to 29%; C5-C6 HCs = 1 to 9%.

Appendix Table 2-1. Component Concentration Ranges for Refinery Gases by CASRN, Gas Name, and TSCA Definition

CAS Number	Petroleum Refinery Gas Name	TSCA Definition	Refinery Gas Composition Ranges
68477-81-6	Gases (petroleum), C6-8 catalytic reformer	A complex combination of hydrocarbons produced by distillation of products from catalytic reforming of C6-C8 feed. It consists of hydrocarbons having carbon numbers in the range of C1 through C5 and hydrogen.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; C1-C4 HCs = 35 to 58.5%; C5-C6 HCs = 0.5 to 5%.
68477-82-7	Gases (petroleum), C6-8 catalytic reformer recycle, hydrogen-rich	No description.	Hydrogen = 50 to 75%; Nitrogen = 1 to 10%; Carbon monoxide = 0.5 to 10%; Carbon dioxide = 0.1 to 3%; Benzene = 0.1 to 2%; C1-C4 HCs = 9 to 20%; C5-C6 HCs = 1 to 10%.
68477-92-9	Gases (petroleum), dry sour, gas-concn.-unit-off	The complex combination of dry gases from a gas concentration unit. It consists of hydrogen, hydrogen sulfide and hydrocarbons having carbon numbers predominantly in the range of C1 through C3.	Hydrogen = 20 to 50%; Nitrogen = 0.5 to 10%; Ammonia = 0.1 to 5%; Hydrogen sulfide = 0.5 to 15%; Methyl mercaptan = 0.1 to 1%; Ethyl mercaptan = 0.01 to 0.5%; C1-C4 HCs = 48 to 79%.
68477-95-2	Gases (petroleum), Girbatol unit feed	A complex combination of hydrocarbons that is used as the feed into the Girbatol unit to remove hydrogen sulfide. It consists of aliphatic hydrocarbons having carbon numbers predominantly in the range of C2 through C4.	Ammonia = 0.01 to 0.5%; Hydrogen sulfide = 0.1 to 4%; Butadiene = 0.1 to 2%; C1-C4 HCs = 93 to 99.8%; C5-C6 HCs = 0.1 to 2%.
68477-97-4	Gases (petroleum), hydrogen-rich	A complex combination separated as a gas from hydrocarbon gases by chilling. It consists primarily of hydrogen with various small amounts of carbon monoxide, nitrogen, methane, and C2 hydrocarbons.	Hydrogen = 65 to 90%; Nitrogen = 1 to 10%; Carbon monoxide = 0.5 to 10%; Carbon dioxide = 0.1 to 3%; C1-C4 HCs = 5 to 15%.
68477-98-5	Gases (petroleum), hydrotreater blend oil recycle, hydrogen-nitrogen-rich	A complex combination obtained from recycled hydrotreated blend oil. It consists primarily of hydrogen and nitrogen with various small amounts of carbon monoxide, carbon dioxide and hydrocarbons having carbon numbers predominantly in the range of C1 through C5.	Hydrogen = 30 to 50%; Nitrogen = 20 to 40%; Carbon monoxide = 0.5 to 20%; Carbon dioxide = 0.1 to 10%; C1-C4 HCs = 0.5 to 18%; C5-C6 HCs = 0.5 to 2%.

Appendix Table 2-1. Component Concentration Ranges for Refinery Gases by CASRN, Gas Name, and TSCA Definition

CAS Number	Petroleum Refinery Gas Name	TSCA Definition	Refinery Gas Composition Ranges
68478-00-2	Gases (petroleum), recycle, hydrogen-rich	A complex combination obtained from recycled reactor gases. It consists primarily of hydrogen with various small amounts of carbon monoxide, carbon dioxide, nitrogen, hydrogen sulfide, and saturated aliphatic hydrocarbons having carbon numbers in the range of C1 through C5.	Hydrogen = 50 to 70%; Nitrogen = 0.5 to 10%; Ammonia = 0.1 to 3%; Hydrogen sulfide = 0.5 to 10%; Carbon monoxide = 0.5 to 10%; Carbon dioxide = 0.1 to 5%; C1-C4 HCs = 4.9 to 13.5%; C5-C6 HCs = 0.1 to 1.5%.
68478-01-3	Gases (petroleum), reformer make-up, hydrogen-rich	A complex combination obtained from the reformers. It consists primarily of hydrogen with various small amounts of carbon monoxide and aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C5.	Hydrogen = 60 to 75%; Nitrogen = 0.5 to 5%; Carbon monoxide = 0.5 to 15%; Carbon dioxide = 0.1 to 5%; C1-C4 HCs = 4.9 to 13.5%; C5-C6 HCs = 0.1 to 1.5%.
68478-02-4	Gases (petroleum), reforming hydrotreater	A complex combination obtained from the reforming hydrotreating process. It consists primarily of hydrogen, methane, and ethane with various small amounts of hydrogen sulfide and aliphatic hydrocarbons having carbon numbers predominantly in the range of C3 through C5.	Hydrogen = 30 to 50%; Nitrogen = 0.5 to 5%; Ammonia = 0.05 to 0.5%; Hydrogen sulfide = 0.1 to 1%; Carbon monoxide = 0.5 to 5%; Carbon dioxide = 0.1 to 3%; C1-C4 HCs = 20 to 49%; C5-C6 HCs = 1 to 10%.
68478-03-5	Gases (petroleum), reforming hydrotreater, hydrogen-methane-rich	A complex combination obtained from the reforming hydrotreating process. It consists primarily of hydrogen and methane with various small amounts of carbon monoxide, carbon dioxide, nitrogen and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of C2 through C5.	Hydrogen = 40 to 60%; Nitrogen = 0.5 to 5%; Ammonia = 0.1 to 2%; Hydrogen sulfide = 0.5 to 5%; Carbon monoxide = 0.5 to 5%; Carbon dioxide = 0.1 to 2%; C1-C4 HCs = 27 to 39.5%; C5-C6 HCs = 0.5 to 3%.
68478-04-6	Gases (petroleum), reforming hydrotreater make-up, hydrogen-rich	A complex combination obtained from the reforming hydrotreating process. It consists primarily of hydrogen with various small amounts of carbon monoxide and aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C5.	Hydrogen = 50 to 75%; Nitrogen = 0.5 to 3%; Ammonia = 0.1 to 1%; Hydrogen sulfide = 0.5 to 3%; Carbon monoxide = 0.5 to 3%; Carbon dioxide = 0.1 to 1%; C1-C4 HCs = 17 to 39.5%; C5-C6 HCs = 0.5 to 3%.

Appendix Table 2-1. Component Concentration Ranges for Refinery Gases by CASRN, Gas Name, and TSCA Definition

CAS Number	Petroleum Refinery Gas Name	TSCA Definition	Refinery Gas Composition Ranges
68478-05-7	Gases (petroleum), thermal cracking distn.	A complex combination produced by distillation of products from a thermal cracking process. It consists of hydrogen, hydrogen sulfide, carbon monoxide, carbon dioxide and hydrocarbons having carbon numbers predominantly in the range of C1 through C6.	Hydrogen = 35 to 50%; Nitrogen = 1 to 5%; Ammonia = 0.1 to 2%; Hydrogen sulfide = 0.5 to 5%; Carbon monoxide = 0.5 to 10%; Carbon dioxide = 0.1 to 5%; Butadiene = 0.1 to 2%; Benzene = 0.1 to 2%; C1-C4 HCs = 20 to 39%; C5-C6 HCs = 1 to 10%.
68478-25-1	Tail gas (petroleum), catalytic cracker refractionation absorber	A complex combination of hydrocarbons obtained from refractionation of products from a catalytic cracking process. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C3.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; C1-C4 HCs = 40 to 59%.
68478-27-3	Tail gas (petroleum), catalytic reformed naphtha separator	A complex combination of hydrocarbons obtained from the catalytic reforming of straight run naphtha. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C6.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; Butadiene = 0.1 to 2%; Benzene = 0.1 to 2%; C1-C4 HCs = 30 to 49%; C5-C6 HCs = 1 to 10%.
68478-28-4	Tail gas (petroleum), catalytic reformed naphtha stabilizer	A complex combination of hydrocarbons obtained from the stabilization of catalytic reformed naphtha. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C6.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%;Butadiene = 0.1 to 2%; Benzene = 0.1 to 2%; C1-C4 HCs = 25 to 56%; C5-C6 HCs = 3 to 15%.
68478-29-5	Tail gas, (petroleum), cracked distillate hydrotreater separator	A complex combination of hydrocarbons obtained by treating cracked distillates with hydrogen in the presence of a catalyst. It consists of hydrogen and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C5.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; C1-C4 HCs = 30 to 58%; C5-C6 HCs = 1 to 10%.
68478-30-8	Tail gas (petroleum), hydrodesulfurized straight-run naphtha separator	A complex combination of hydrocarbons obtained from hydrodesulfurization of straight-run naphtha. It consists of hydrogen and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C6.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; C1-C4 HCs = 25 to 56%; C5-C6 HCs = 3 to 15%.

Appendix Table 2-1. Component Concentration Ranges for Refinery Gases by CASRN, Gas Name, and TSCA Definition

CAS Number	Petroleum Refinery Gas Name	TSCA Definition	Refinery Gas Composition Ranges
68513-11-1	Fuel gases, hydrotreater fractionation, scrubbed	A complex combination produced by the fractionation and scrubbing of products from various hydrotreating units. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C4.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; C1-C4 HCs = 40 to 59%.
68513-13-3	Fuel gases, thermal cracked catalytic cracking residue	A complex combination obtained by the thermal cracking of a catalytically cracked residuum. It consists of hydrogen and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C4.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; C1-C4 HCs = 40 to 59%.
68513-14-4	Gases (petroleum), catalytic reformed straight-run naphtha stabilizer overheads	A complex combination of hydrocarbons obtained from the catalytic reforming of straight-run naphtha followed by fractionation of the total effluent. It consists of hydrogen, methane, ethane and propane.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; C1-C4 HCs = 40 to 59%.
68513-16-6	Gases (petroleum), hydrocracking depropanizer off, hydrocarbon-rich	A complex combination of hydrocarbons produced by the distillation of products from a hydrocracking process. It consists predominantly of hydrocarbons having carbon numbers predominantly in the range of C1 through C4. It may also contain small amounts of hydrogen and hydrogen sulfide.	Hydrogen = 1 to 10%; Nitrogen = 0.1 to 0.5%; Ammonia = 0.01 to 0.2%; Hydrogen sulfide = 0.1 to 0.5%; Butadiene = 0.1 to 2%; C1-C4 HCs = 89 to 98%.
68513-18-8	Gases (petroleum), reformer effluent high-pressure flash drum off	A complex combination produced by the high-pressure flashing of the effluent from the reforming reactor. It consists primarily of hydrogen with various small amounts of methane, ethane, and propane.	Hydrogen = 50 to 74%; Nitrogen = 1 to 5%; C1-C4 HCs = 25 to 49%.
68513-19-9	Gases (petroleum), reformer effluent low-pressure flash drum off	A complex combination produced by the low-pressure flashing of the effluent from the reforming reactor. It consists primarily of hydrogen with various small amounts of methane, ethane, and propane.	Hydrogen = 50 to 74%; Nitrogen = 1 to 5%; C1-C4 HCs = 25 to 49%.
68513-68-8	Residues (petroleum), deethanizer tower	A complex residuum from the distillation of a gas stream containing hydrogen, carbon monoxide, carbon dioxide and hydrocarbons having carbon numbers in the range of C1 through C6 or from the cracking of ethane and propane. It consists of hydrocarbons having carbon	Butadiene = 0.01 to 1%; Benzene = 0.05 to 1%; C1-C4 HCs = 80 to 95%; C5-C6 HCs = 5 to 20%.

Appendix Table 2-1. Component Concentration Ranges for Refinery Gases by CASRN, Gas Name, and TSCA Definition			
CAS Number	**Petroleum Refinery Gas Name**	**TSCA Definition**	**Refinery Gas Composition Ranges**
		numbers in the range of C2 through C6. It may contain small amounts of benzene.	
68527-13-9	Gases, (petroleum), acid, ethanolamine scrubber	A complex mixture separated from refinery gas by scrubbing with ethanolamine. It consists primarily of hydrogen sulfide and carbon dioxide. It may also contain various small amounts of hydrogen, carbon monoxide and nitrogen.	Hydrogen = 1 to 10%; Nitrogen = 1 to 10%; Ammonia = 1 to 10%; Hydrogen sulfide = 35 to 45%; Carbon monoxide = 1 to 10%; Carbon dioxide = 35 to 45%.
68527-14-0	Gases, (petroleum), methane-rich off ..C1	A complex combination separated by distillation of a gas stream containing hydrogen, carbon monoxide, carbon dioxide and hydrocarbons having carbon numbers in the range of C1 through C6 or obtained by the cracking of ethane and propane. It consists primarily of methane with various small amounts of hydrogen and nitrogen.	Hydrogen = 10 to 20%; Nitrogen = 10 to 20%; C1-C4 HCs = 60 to 80%.
68527-15-1	Gases (petroleum), oil refinery gas distn. off	A complex combination separated by distillation of a gas containing hydrogen, carbon monoxide, carbon dioxide and hydrocarbons having carbon numbers in the range of C1 through C6 or obtained by cracking ethane and propane. It consists of hydrocarbons having carbon numbers predominantly in the range of C1 through C2, hydrogen, nitrogen, and carbon monoxide.	Hydrogen = 30 to 45%; Nitrogen = 5 to 20%; Carbon monoxide = 0.5 to 20%; Carbon dioxide = 0.1 to 10%; C1-C4 HCs = 30 to 45%.
68602-82-4	Gases (petroleum), benzene unit hydrotreater depentanizer overheads	A complex combination produced by treating the feed from the benzene unit with hydrogen in the presence of a catalyst followed by depentanizing. It consists primarily of hydrogen, ethane and propane with various small amounts of nitrogen, carbon monoxide, carbon dioxide, and hydrocarbons having carbon numbers predominantly in the range of C1 through C6. It may contain trace amounts of benzene.	Hydrogen = 40 to 60%; Nitrogen = 1 to 10%; Carbon monoxide = 0.5 to 10%; Carbon dioxide = 0.1 to 3%; Benzene = 0.1 to 1%; C1-C4 HCs = 27 to 35%; C5-C6 HCs = 3 to 15%.

Appendix Table 2-1. Component Concentration Ranges for Refinery Gases by CASRN, Gas Name, and TSCA Definition

CAS Number	Petroleum Refinery Gas Name	TSCA Definition	Refinery Gas Composition Ranges
68602-84-6	Gases (petroleum), secondary absorber off, fluidized catalytic cracker overheads fractionator	A complex combination produced by the fractionation of the overhead products from the catalytic cracking process in the fluidized catalytic cracker. It consists primarily of hydrogen, nitrogen, and hydrocarbons having carbon numbers predominantly in the range of C1 through C3.	Hydrogen = 35 to 45%; Nitrogen = 10 to 30%; C1-C4 HCs = 35 to 45%.
68607-11-4	Petroleum products, refinery gases	A complex combination which consists primarily of hydrogen with various small amounts of methane, ethane, and propane.	Hydrogen = 55 to 74%; Nitrogen = 1 to 5%; C1-C4 HCs = 21 to 44%.
68783-05-1	Gases, (petroleum), ammonia-hydrogen sulfide, water-satd.	A water-saturated gas produced by the treatment of waste process water through steam stripping. It consists of up to 30% hydrogen sulfide and up to 60% ammonia.	Hydrogen = 1 to 5%; Nitrogen = 1 to 10%; Ammonia = 45 to 60%; Hydrogen sulfide = 20 to 30%; Water = 1 to 5%.
68783-06-2	Gases (petroleum), hydrocracking low-pressure separator	A complex combination obtained by the liquid-vapor separation of the hydrocracking process reactor effluent. It consists predominantly of hydrogen and saturated hydrocarbons having carbon numbers predominantly in the range of C1 through C3.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; C1-C4 HCs = 40 to 59%.
68783-07-3	Gases (petroleum), refinery blend	A complex combination obtained from various refinery processes. It consists of hydrogen, hydrogen sulfide and hydrocarbons having carbon numbers predominantly in the range of C1 through C5.	Hydrogen = 1 to 15%; Nitrogen = 0.05 to 5%; Ammonia = 0.1 to 1%; Hydrogen sulfide = 0.1 to 4%; Methyl mercaptan = 0.1 to 0.5%; Ethyl mercaptan = 0.01 to 0.1%; Carbon monoxide = 0.5 to 5%; Carbon dioxide = 0.1 to 3%; Butadiene = 0.1 to 2%; C1-C4 HCs = 58 to 80%; C5-C6 HCs = 1 to 10%.
68783-62-0	Fuel gases, refinery, unsweetened	A complex combination obtained by the fractionation of naphtha and compressed hydrocarbon gas streams from various refinery processes. It consists predominantly of hydrocarbons having carbon numbers predominantly in the range of C1 through C5 and boiling in the range of -73.degrees C to 65.degrees C (-100.degrees F to 150.degrees F).	Hydrogen = 0.1 to 5%; Nitrogen = 0.05 to 5%; Ammonia = 0.1 to 1%; Hydrogen sulfide = 0.1 to 4%; Methyl mercaptan = 0.1 to 1%; Ethyl mercaptan = 0.01 to 0.5%; Carbon monoxide = 0.5 to 5%; Carbon dioxide = 0.1 to 3%; Butadiene = 0.1 to 2%; C1-C4 HCs = 61 to 94%; C5-C6 HCs = 1 to 15%.

Appendix Table 2-1. Component Concentration Ranges for Refinery Gases by CASRN, Gas Name, and TSCA Definition

CAS Number	Petroleum Refinery Gas Name	TSCA Definition	Refinery Gas Composition Ranges
68814-47-1	Waste gases, refinery vent	A complex combination obtained from various refinery processes. It consists of hydrocarbons having carbon numbers predominantly in the range of C1 through C5 and hydrogen sulfide.	Hydrogen = 1 to 5%; Nitrogen = 1 to 10%; Ammonia = 1 to 15%; Hydrogen sulfide = 20 to 35%; Butadiene = 0.1 to 2%; C1-C4 HCs = 25 to 49%; C5-C6 HCs = 1 to 10%.
68814-67-5	Gases (petroleum), refinery	A complex combination obtained from various petroleum refining operations. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C3.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; C1-C4 HCs = 40 to 59%.
68814-90-4	Gases (petroleum), platformer products separator off	A complex combination obtained from the chemical reforming of naphthenes to aromatics. It consists mainly of hydrogen and saturated hydrocarbons having carbon numbers predominantly in the range of C2 through C4.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; C1-C4 HCs = 40 to 59%.
68911-58-0	Gases (petroleum), hydrotreated sour kerosine depentanizer stabilizer off	The complex combination obtained from the depentanizer stabilization of hydrotreated kerosine. It consists primarily of hydrogen, methane, ethane, and propane with various small amounts of nitrogen, hydrogen sulfide, carbon monoxide and hydrocarbons having carbon numbers predominantly in the range of C4 through C5.	Hydrogen = 35 to 50%; Nitrogen = 1 to 5%; Ammonia = 0.1 to 2%; Hydrogen sulfide = 0.5 to 5%; Carbon monoxide = 0.5 to 5%; Carbon dioxide = 0.1 to 3%; C1-C4 HCs = 25 to 44%; C5-C6 HCs = 1 to 10%.
68911-59-1	Gases (petroleum), hydrotreated sour kerosine flash drum	A complex combination obtained from the flash drum of the unit treating sour kerosine with hydrogen in the presence of a catalyst. It consists primarily of hydrogen and methane with various small amounts of nitrogen, carbon monoxide, and hydrocarbons having carbon numbers predominantly in the range of C2 through C5.	Hydrogen = 40 to 50%; Nitrogen = 1 to 5%; Carbon monoxide = 0.5 to 5%; Carbon dioxide = 0.1 to 3%; C1-C4 HCs = 30 to 49%; C5-C6 HCs = 1 to 10%.
68919-01-7	Gases (petroleum), distillate unifiner desulfurization stripper off	A complex combination stripped from the liquid product of the unifiner desulfurization process. It consists of hydrogen sulfide, methane, ethane, and propane.	Hydrogen = 1 to 5%; Nitrogen = 1 to 5%; Ammonia = 1 to 15%; Hydrogen sulfide = 25 to 45%; C1-C4 HCs = 40 to 55%.

Appendix Table 2-1. Component Concentration Ranges for Refinery Gases by CASRN, Gas Name, and TSCA Definition

CAS Number	Petroleum Refinery Gas Name	TSCA Definition	Refinery Gas Composition Ranges
68919-02-8	Gases (petroleum), fluidized catalytic cracker fractionation off	A complex combination produced by the fractionation of the overhead product of the fluidized catalytic cracking process. It consists of hydrogen, hydrogen sulfide, nitrogen, and hydrocarbons having carbon numbers predominantly in the range of C1 through C5.	Hydrogen = 35 to 45%; Nitrogen = 1 to 15%; Ammonia = 0.1 to 5%; Hydrogen sulfide = 1 to 15%; Butadiene = 0.1 to 2%; C1-C4 HCs = 25 to 44%; C5-C6 HCs = 1 to 10%.
68919-03-9	Gases (petroleum), fluidized catalytic cracker scrubbing secondary absorber off	A complex combination produced by scrubbing the overhead gas from the fluidized catalytic cracker. It consists of hydrogen, nitrogen, methane, ethane and propane.	Hydrogen = 40 to 55%; Nitrogen = 1 to 20%; C1-C4 HCs = 40 to 54%.
68919-04-0	Gases (petroleum), heavy distillate hydrotreater desulfurization stripper off	A complex combination stripped from the liquid product of the heavy distillate hydrotreater desulfurization process. It consists of hydrogen, hydrogen sulfide, and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C5.	Hydrogen = 35 to 45%; Nitrogen = 1 to 15%; Ammonia = 0.1 to 5%; Hydrogen sulfide = 1 to 15%; C1-C4 HCs = 25 to 44%; C5-C6 HCs = 1 to 10%.
68919-07-3	Gases (petroleum), platformer stabilizer off, light ends fractionation	A complex combination obtained by the fractionation of the light ends of the platinum reactors of the platformer unit. It consists of hydrogen, methane, ethane, and propane.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; C1-C4 HCs = 40 to 59%.
68919-08-4	Gases (petroleum), preflash tower off, crude distn.	A complex combination produced from the first tower used in the distillation of crude oil. It consists of nitrogen and saturated aliphatic hydrocarbons having carbon numbers predominantly in the range of C1 through C5.	Hydrogen = 1 to 10%; Nitrogen = 20 to 50%; Ammonia = 0.01 to 0.5%; Hydrogen sulfide = 0.05 to 0.2%; C1-C4 HCs = 25 to 54%; C5-C6 HCs = 5 to 15%.
68919-12-0	Gases (petroleum), unifiner stripper off	A combination of hydrogen and methane obtained by fractionation of the products from the unifiner unit.	Hydrogen = 40 to 55%; Nitrogen = 1 to 5%; C1-C4 HC = 40 to 54%.
68952-79-4	Tail gas (petroleum), catalytic hydrodesulfurized naphtha separator	A complex combination of hydrocarbons obtained from the hydrodesulfurization of naphtha. It consists of hydrogen, methane, ethane, and propane.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; C1-C4 HCs = 40 to 59%.
68952-80-7	Tail gas (petroleum), straight-run naphtha hydrodesulfurizer	A complex combination obtained from the hydrodesulfurization of straight-run naphtha. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C5.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; Butadiene = 0.1 to 2%; C1-C4 HCs = 30 to 58%; C5-C6 HCs = 1 to 10%.

Appendix Table 2-1. Component Concentration Ranges for Refinery Gases by CASRN, Gas Name, and TSCA Definition			
CAS Number	**Petroleum Refinery Gas Name**	**TSCA Definition**	**Refinery Gas Composition Ranges**
68955-33-9	Gases (petroleum), sponge absorber off, fluidized catalytic cracker and gas oil desulfurizer overhead fractionation	A complex combination obtained by the fractionation of products from the fluidized catalytic cracker and gas oil desulfurizer. It consists of hydrogen and hydrocarbons having carbon numbers predominantly in the range of C1 through C4.	Hydrogen = 40 to 59%; Nitrogen = 1 to 5%; Butadiene = 0.1 to 2%; C1-C4 HCs = 40 to 59%.
68989-88-8	Gases (petroleum), crude distn. and catalytic cracking	A complex combination produced by crude distillation and catalytic cracking processes. It consists of hydrogen, hydrogen sulfide, nitrogen, carbon monoxide and paraffinic and olefinic hydrocarbons having carbon numbers predominantly in the range of C1 through C6.	Hydrogen = 30 to 45%; Nitrogen = 1 to 10%; Ammonia = 0.1 to 5%; Hydrogen sulfide = 0.5 to 10%; Carbon monoxide = 0.5 to 10%; Carbon dioxide = 0.1 to 5%; Butadiene = 0.1 to 2%; Benzene = 0.1 to 2%; C1-C4 HCs = 25 to 44%; C5-C6 HCs = 1 to 10%.

To more easily see what components are present in each refinery stream, and at what concentration ranges, the same data presented in Appendix Table 2.1 (above) is presented by CASRN and constituent components in Appendix Table 2.2 below.

Appendix Table 2-2. Component Concentration Ranges for Refinery Gases by CASRN and Component Ranges

CASRN		Component Compositional Ranges[1] (% weight/volume)										
				Mercaptans		Asphyxiant Gases			Hydrocarbons			
	Ammonia	Carbon Monoxide	Hydrogen Sulfide	Methane-thiol	Ethane-thiol	Carbon dioxide	Hydrogen	Nitrogen	Benzene	1,3-Butadiene	C1 – C4 Hydro-Carbons	C5 – C6 Hydro-Carbons
8006-20-0		20 - 30				20 - 30	20 - 30	20 - 30			1 - 10	
68308-27-0							40 - 59	1 - 5		0.1 - 2	37 – 58.5	0.5 - 3
68476-26-6	0.01-0.2	0.5 - 5	0.01 - 0.5			0.1 - 3	40 - 88	1 - 5			10 - 58	
68476-27-7		0.5 - 5				0.1 - 3	40 - 59	0.5 - 5			37 – 49.5	0.5 - 3
68476-28-8		0.5 - 10				0.1 - 5	35 - 45	1 - 10			25 - 40	5 - 10
68476-29-9							40 - 59	1 - 5		0.1 - 2	40 - 59	
68477-65-6	0.1 - 10	0.5 - 15	10 - 25			0.1 - 10	30 - 50				0.9 - 9	0.1 - 1
68477-66-7		0.5 - 20				0.1 - 10	50 - 75		0.1 - 2		0.3 - 13	0.7 - 7
68477-67-8		0.5 - 15				0.1 - 5	60 - 80		0.1 - 2		0.3 - 13	0.7 - 7
68477-68-9		0.5 - 20				0.1 - 10	30 - 50	20 - 40			0.9 - 18	. 1 - 2
68477-77-0							40 - 60				40 - 60	
68477-80-5		0.5 - 15				0.1 - 5	40 - 60	1 - 15	0.1 - 2		1 - 29	1 - 9
68477-81-6							40 - 59	1 - 5			35 – 58.5	0.5 - 5
68477-82-7		0.5 - 10				0.1 - 3	50 - 75	1 - 10	0.1 - 2		9 - 20	1 - 10
68477-92-9	0.1 - 5		0.5 - 15	0.1 - 1	0.01 - 0.5		20 - 50	0.5 - 10			48 - 79	
68477-95-2	0.01 - 0.5		0.1 - 4							0.1 - 2	93 - 99.8	0.1 - 2
68477-97-4		0.5 - 10				0.1 - 3	65 - 90	1 - 10			5 - 15	
68477-98-5		0.5 - 20				0.1 - 10	30 - 50	20 - 40			0.5 - 18	0.5 - 2
68478-00-2	0.1 - 3	0.5 - 10	0.5 - 10			0.1 - 5	50 - 70	0.5 - 10			4.9 – 13.5	0.1 – 1.5

[1] a blank cell indicates that the component is not present in that stream.

Appendix Table 2-2. Component Concentration Ranges for Refinery Gases by CASRN and Component Ranges

CASRN		Component Compositional Ranges[1] (% weight/volume)										
				Mercaptans		Asphyxiant Gases			Hydrocarbons			
	Ammonia	Carbon Monoxide	Hydrogen Sulfide	Methane-thiol	Ethane-thiol	Carbon dioxide	Hydrogen	Nitrogen	Benzene	1,3-Butadiene	C1 – C4 Hydro-Carbons	C5 – C6 Hydro-Carbons
68478-01-3		0.5 - 15				0.1 - 5	60 - 75	0.5 - 5			4.9 – 13.5	0.1 – 1.5
68478-02-4	0.05 - 0.5	0.5 - 5	0.1 - 1			0.1 - 3	30 - 50	0.5 - 5			20 - 49	1 - 10
68478-03-5	0.1 - 2	0.5 - 5	0.5 - 5			0.1 - 2	40 - 60	0.5 - 5			27 – 39.5	0.5 - 3
68478-04-6	0.1 - 1	0.5 - 3	0.5 - 3			0.1 - 1	50 - 75	0.5 - 3			17 – 39.5	0.5 - 3
68478-05-7	0.1 - 2	0.5 - 10	0.5 - 5			0.1 - 5	35 - 50	1 - 5	0.1 - 2	0.1 - 2	20 - 39	1 - 10
68478-25-1							40 - 59	1 - 5			40 - 59	
68478-27-3							40 - 59	1 - 5	0.1 - 2	0.1 - 2	30 - 49	1 - 10
68478-28-4							40 - 59	1 - 5	0.1 - 2	0.1 - 2	25 - 56	3 - 15
68478-29-5							40 - 59	1 - 5			30 - 58	1 - 10
68478-30-8							40 - 59	1 - 5			25 - 56	3 - 15
68513-11-1							40 - 59	1 - 5			40 - 59	
68513-13-3							40 - 59	1 - 5			40 - 59	
68513-14-4							40 - 59	1 - 5			40 - 59	
68513-16-6	0.01 - 0.2		0.1 - 0.5				1 - 10	0.1 - 0.5		0.1 - 2	89 - 98	
68513-18-8							50 - 74	1 - 5			25 - 49	
68513-19-9							50 - 74	1 - 5			25 - 49	
68513-68-8									0.05 - 1	0.01 - 1	80 - 95	5 - 20
68527-13-9	1 - 10	1 - 10	35 - 45			35 - 45	1 - 10	1 - 10				
68527-14-0							10 - 20	10 - 20			60 - 80	
68527-15-1		0.5 - 20				0.1 - 10	30 - 45	5 - 20			30 - 45	
68602-82-4		0.5 - 10				0.1 - 3	40 - 60	1 - 10	0.1 - 1		27 - 35	3 - 15
68602-84-6							35 - 45	10 - 30			35 - 45	
68607-11-4							55 - 74	1 - 5			21 - 44	
68783-05-1	45 - 60		20 - 30				1 - 5	1 - 10				
68783-06-2							40 - 59	1 - 5			40 - 59	

Appendix Table 2-2. Component Concentration Ranges for Refinery Gases by CASRN and Component Ranges

CASRN		Component Compositional Ranges[1] (% weight/volume)										
				Mercaptans		Asphyxiant Gases			Hydrocarbons			
	Ammonia	Carbon Monoxide	Hydrogen Sulfide	Methane-thiol	Ethane-thiol	Carbon dioxide	Hydrogen	Nitrogen	Benzene	1,3-Butadiene	C1 – C4 Hydro-Carbons	C5 – C6 Hydro-Carbons
68783-07-3	0.1 - 1	0.5 - 5	0.1 - 4	0.1 - 0.5	0.01 - 0.1	0.1 - 3	1 - 15	0.05 - 5		0.1 - 2	58 - 80	1 - 10
68783-62-0	0.1 - 1	0.5 - 5	0.1 - 4	0.1 - 1	0.01 - 0.5	0.1 - 3	0.1 - 5	0.05 - 5		0.1 - 2	61 - 94	1 - 15
68814-47-1	1 - 15		20 - 35				1 - 5	1 - 10		0.1 - 2	25 - 49	1 - 10
68814-67-5							40 - 59	1 - 5			40 - 59	
68814-90-4							40 - 59	1 - 5			40 - 59	
68911-58-0	0.1 - 2	0.5 - 5	0.5 - 5			0.1 - 3	35 - 50	1 - 5			25 - 44	1 - 10
68911-59-1		0.5 - 5				0.1 - 3	40 - 50	1 - 5			30 - 49	1 - 10
68919-01-7	1 - 15		25 - 45				1 - 5	1- 5			40 - 55	
68919-02-8	0.1 - 5		1 - 15				35 - 45	1 - 15		0.1 - 2	25 - 44	1 - 10
68919-03-9							40 - 55	1 - 20			40 - 54	
68919-04-0	0.1 - 5		1 - 15				35 - 45	1 - 15			25 - 44	1 - 10
68919-07-3							40 - 59	1 - 5			40 - 59	
68919-08-4	0.01 - 0.5		0.05 -0.2				1 - 10	20 - 50			25 - 54	5 - 15
68919-12-0							40 - 55	1 - 5			40 – 54	
68952-79-4							40 - 59	1 - 5			40 - 59	
68952-80-7							40 - 59	1 - 5		0.1 - 2	30 – 58	1 - 10
68955-33-9							40 - 59	1 - 5		0.1 - 2	40 - 59	
68989-88-8	0.1 - 5	0.5 - 10	0.5 - 10			0.5 - 10	30-45	1 - 10	0.1 - 2	0.1 - 2	25 - 44	1 - 10

Appendix 3

Key Studies for Refinery Gases Hydrocarbon and Inorganic Constituents

ACUTE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LC50/LD50**	**Reference**	**Comments**
C1-C4 (2-Butene has lowest LC50 for this category)	107-07-7	Inhalation	Rat	>10,000 ppm	Arts, JHE. 1992. Acute (4-hour) inhalation toxicity study of butene-2 in rats. Report No. V92.183/352130. TNO Nutrition and Food Research, Zeist, The Netherlands. [2butene]	OECD limit test
methane ethane propane butane isobutane	74-82-8 74-84-0 74-98-6 106-97-8 75-28-5	Aqueous	fish invertebrate algae	11 – 167 ppm 13 – 164 ppm 1.3 – 96 ppm	EPA (U.S. Environmental Protection Agency). 2000. EPI Suite™, the Estimation Programs Interface (EPI) Suite™. U.S. Environmental Protection Agency, Washington, DC.	Ranges of values represent structure-activity modelling using the ECOSAR Program in EPI Suite™. Chemical list includes C1-C4 compounds methane, ethane, propane, butane, isobutane, and 1,3-butadiene. .

ACUTE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LC50/LD50**	**Reference**	**Comments**
C5-C6	Several; see gasoline blending streams Category Analysis Document, 2008	Inhalation	Rat	LC50>1063 ppm	API (American Petroleum Institute) 1980. Acute toxicity tests. API PS-6 unleaded motor gasoline. API Rpt #27-32130, Washington, DC. API (American Petroleum Institute) 1984. Acute inhalation toxicity evaluation of a petroleum derived hydrocarbon in rats. API 83-05 Full range catalytic reformed naphtha. API Rpt. #31-30681. Washington, DC. API (American Petroleum Institute) 1987a. Acute inhalation toxicity evaluation of a petroleum derived hydrocarbon in rats. API 83-19 Light alkylate naphtha. API Rpt. #34-30636. Washington, DC. API (American Petroleum Institute) 1987b. Acute inhalation toxicity evaluation of a petroleum derived hydrocarbon in rats. API 83-20 Light catalytic cracked naphtha. API Rpt. #34-32777. Washington, DC. API (American Petroleum Institute) 1987c. Acute inhalation toxicity evaluation of a petroleum derived hydrocarbon in rats. API 81-08 Sweetened naphtha. API Rpt #33-31827. Washington, DC.	Weight of evidence from four gasoline blending streams (high paraffinic stream, high olefinic stream , high naphthenic stream, and high aromatic stream) plus wholly vaporized gasoline)
pentane hexane	109-66-0 110-54-3	Aqueous	fish invertebrate algae	3.9 – 9.5 ppm 4.6 – 11 ppm 3.1 – 7.0 ppm	EPA (U.S. Environmental Protection Agency). 2000. EPI Suite™, the Estimation Programs Interface (EPI) Suite™. U.S. Environmental Protection Agency, Washington, DC.	Ranges of values represent structure-activity modelling using the ECOSAR Program in EPI Suite™. Chemical list includes C5-C6 compounds pentane and hexane.

ACUTE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LC50/LD50**	**Reference**	**Comments**
Nitrogen	7727-37-9	No specific data; considered a simple asphyxiant			McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.
Hydrogen	1333-74-0	No specific data; considered a simple asphyxiant			McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.
Carbon Dioxide	124-38-9	No specific data; considered a simple asphyxiant			McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.

ACUTE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LC50/LD50**	**Reference**	**Comments**
1,3-Butadiene	106-99-0	Inhalation	Rat	129,000 ppm (4 hr)	Shugaev, BB. 1969. Concentrations of hydrocarbons in tissues as a measure of toxicity. Arch. Environ. Health 18:878882.	Study used to support IDLH.
		Aqueous	Fish Invertebrate Algae	38 ppm 40 ppm 25 ppm	EPA (U.S. Environmental Protection Agency). 2000. EPI Suite™, the Estimation Programs Interface (EPI) Suite™. U.S. Environmental Protection Agency, Washington, DC.	
Benzene	71-43-2	Inhalation	Rat	13,700 ppm (4 hr)	Drew RT and JR Fouts. 1974. The lack of effects of pretreatment with phenobarbital and chlorpromazine on the acute toxicity of benzene in rats. Toxicol Appl Pharmacol 27:183-193.	
		Aqueous	Fish Invertebrate Algae	5.3 ppm 59.6 ppm 29 ppm	DeGraeve, GM, Elder, RG, Woods, DC and HL Bergman. 1982. Effects of naphthalene and benzene on fathead minnows and rainbow trout. Arch. Environ. Contam. Toxicol. 11(4):487-490. MacLean, MM. and KG Doe. 1989. The Comparative Toxicity of Crude and Refined Oils to Daphnia magna and Artemia. Environment Canada, EE-111, Dartmouth, Nova Scotia. 64 p. Galassi, SM, Mingazzini, L, . Vigano, D, Cesaeeo, and ML Tosato. 1988. Approaches to Modeling the Toxic Responses of Aquatic Organisms to Aromatic Hydrocarbons. Ecotoxicol. Environ. Saf. 16(2):158-169.	

ACUTE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LC50/LD50**	**Reference**	**Comments**
Methyl Mercaptan	74-93-1	Inhalation	Rat	675 ppm (4 hr)	Tansy MF, Kendall, FM, Fantasia, J, Landin, WE and R Oberly. 1981. Acute and subchronic toxicity studies of rats exposed to vapors of methyl mercaptan and other reduced-sulfur compounds. J Toxicol Environ Health, 8, 71-88.	
		Aqueous	Fish	0.5< LC50 <1.75 ppm	Haydu, EP, et al. 1952 The effect of kraft mill waste components on certain salmonoid fishes of the Pacific Northwest. TAPPI. 35(12):545-549.	
			Invertebrate	1.32< EC50 <2.46 ppm	Elf Atochem SA. 2000. Methyl mercaptans 33% sodium: acute toxicity to daphnias. Centre d/Application de Levallois. Study No. 604/99/A.	
			Algae	no data		
Ethyl Mercaptan	75-08-01	Inhalation	Mice	2770 ppm (4 hr)	Fairchild, EJ and HE Stokinger. 1958. Toxicologic studies on organic sulfur compounds. I. Acute toxicity of some aliphatic and aromatic thiols (Mercaptans). Am. Ind. Hyg. Assoc. J. 19:171-189.	

ACUTE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LC50/LD50**	**Reference**	**Comments**
		Aqueous	Fish Invertebrate Algae	1.6 ppm 90 – 280 ppm no data	EPA (U.S. Environmental Protection Agency). 2000. EPI Suite™, the Estimation Programs Interface (EPI) Suite™. U.S. Environmental Protection Agency, Washington, DC. Maas, JL. 1990. Toxicity research with thiourea. Laboratory for Ecotoxicology. Institute for Inland Water Management and Waste Water Treatment, Report No. AOCE: 4p (DUT)	
Ammonia	7664-41-7	Inhalation	Mice	4230 ppm (1 hr)	Kapeghian, JC, Mincer, HH, Jones, AL, Verlangieri, AJ, and IW Waters. 1982. Acute inhalation toxicity of ammonia in mice. Bull Environ Contam Toxicol 29:371-378.	Used to support AEGL value
		Aqueous	Fish Invertebrate Algae	0.083 – 4.6 ppm 0.53 – 22.8 ppm no data	US EPA (United States Environmental Protection Agency). 1986. Quality Criteria for Water: 1986. EPA 440/5-86-001, U.S. EPA, Office of Water, Washington, DC.	
Hydrogen Sulfide	7783-06-4	Inhalation	Rat	444 ppm (4 hr)	Tansy MF, Kendall, FM, Fantasia, J, Landin, WE and R Oberly. 1981. Acute and subchronic toxicity studies of rats exposed to vapors of methyl mercaptan and other reduced-sulfur compounds. J Toxicol Environ Health, 8, 71-88.	

ACUTE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LC50/LD50**	**Reference**	**Comments**
		Aqueous	Fish Invertebrate Algae	0.007 ppm 0.204 ppm no data	Fung, DK, and PH Bewick. 1980. Short-Term Toxicity of Aqueous Hydrogen Sulfide to Representative Fish Species of Lake Huron. In: Eaton, J.G., P.R. Parrish, and A.C. Hendricks (Eds.), Aquatic Toxicology and Hazard Assessment, 3rd Symposium, ASTM STP 707, Philadephia, PA. Smith, LL, Jr. and DM. Oseid. 1975 Chronic Effects of Low Levels of Hydrogen Sulfide on Freshwater Fish. Prog. Water Technol. 7(3/4):599-605.	
Carbon Monoxide	630-08-0	Inhalation	Rat	1807 ppm (4 hr)	Rose CS, Jones, RA, Jenkins, LJ Jr, and J Siegel. 1970. The acute hyperbaric toxicity of carbon monoxide. Toxicol Appl Pharmacol *17*:752760.	
		Aqueous	Fish Invertebrate Algae	no specific data, considered asphyxiant		

REPEAT DOSE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LOAEL/ Duration**	**Reference**	**Comments**
C1-C4 (2-Butene has lowest LOAEL for this group of consituents)	107-07-7	Inhalation	Rat	5000 ppm/ 39-46 days	Waalkens-Brendsen, DH. and JHE Arts. 1992. Combined short term inhalation and reproductive/developmental toxicity screening test with Butene-2 in rats. Proj. #B91-8336 (Study #1410) [2-butene].	Body weight decrease
C5-C6	Several; see gasoline blending streams Category Analysis Document, 2008	Inhalation	Rat	6625 ppm/ 13 weeks	API (American Petroleum Institute) 2005a. Baseline Gasoline Vapor Condensate A 13 week whole body inhalation toxicity Study in Rats with Neurotoxicity Assessments and 4-week In Vivo Genotoxicty and Immunotoxicity Assessments. HLS Study No. 00-6125. Huntingdon Life Sciences Laboratories, East Millstone, NJ.	
Nitrogen	7727-37-9	No specific data; considered a simple asphyxiant			McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.

REPEAT DOSE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LOAEL/ Duration**	**Reference**	**Comments**
Hydrogen	1333-74-0	No specific data; considered a simple asphyxiant			McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.
Carbon Dioxide	124-38-9	No specific data; considered a simple asphyxiant			McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.

REPEAT DOSE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LOAEL/ Duration**	**Reference**	**Comments**
1,3-Butadiene	106-99-0	Inhalation	Rat	8000 ppm / 105 wks	Owen, PE. 1981. The toxicity and carcinogenicity of butadiene gas administered to rats by inhalation for approximately 24 months. Report No. 2653-522/2. Harrogate, Hazleton Laboratories Europe Ltd. (Confidential report prepared for the International Institute of Synthetic Rubber Producers Inc., New York, USA). Owen PE and JR Glaister. 1990. Inhalation toxicity and carcinogenicity of 1,3-butadiene in Sprague-Dawley rats. Environ Health Persp. **86;** 19-25. Owen PE, Glaister, JR, Gaunt, IF, and DH Pullinger.1987. Inhalation toxicity studies with 1,3-butadiene. 3. Two year toxicity/ carcinogenicity study in rats. Am Ind Hyg Assoc J. **48;** 407-413.	Note: butadiene classified as a human carcinogen
Benzene	71-43-2	Inhalation	Mice	≤10 ppm/ 50 days	Green, JD, Snyder, CA, LoBue J, Goldstein, BD, and RE Albert. 1981. Acute and chronic dose/response effect of benzene inhalation on the peripheral blood, bone marrow, and spleen cell of CD-1 male mice. Toxicol Appl Pharmacol 59:204-214.	Increases in splenic weight and cellularity.
Methyl Mercaptan	74-93-1	Inhalation	Rat	57 ppm/ 90 day	Tansy MF, Kendall, FM, Fantasia, J, Landin, WE and R Oberly. 1981. Acute and subchronic toxicity studies of rats exposed to vapors of methyl mercaptan and other reduced-sulfur compounds. J Toxicol Environ Health, 8, 71-88.	Body weight decrease

REPEAT DOSE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LOAEL/ Duration**	**Reference**	**Comments**
Ethyl Mercaptan		No Data – read across from methyl mercaptan				
Ammonia	7664-41-7	Inhalation	Rat	90 ppm/ 50 days	Stolpe, J, and R Sedlag. 1976; Die Einzel- und Komplexwirkung von Ammoniak und Schwefelwasserstoff in der Luft auf kleine Versuchstiere (Ratten) bei unterschiedlichen Umweltbedingungen; Ach. Exper. Vet. Med. 30, 533-539.	Increased haemoglobin, and haemotocrit KS=4; The information given is limited. However, a well-conducted feeding study in rats on diammonium phosphate resulted in no observable subchronic effects. Another well-conducted repeat dose study in rats on ammonium sulfate also did not result in effects .
Hydrogen Sulfide	7783-06-4	Inhalation	Rat	30 ppm/ 90 day	Dorman, DC, Struve, MF, Gross, EA, and KA Brenneman. 2004. Respiratory tract toxicity of inhaled hydrogen sulfide in Fischer-344 rats, Sprague-Dawley rats, and B6C3F1 mice following subchronic (90-day) exposure. Toxicol. Appl. Pharmacol. 198(1):29-39. Brenneman, KA, James, RA, Gross, EA, Dorman, DC. (2000) Olfactory loss in adult male CD rats following inhalation exposure to hydrogen sulfide. Toxicologic Pathology 28(2): 326-333. CIIT. Toxigenics, Inc. 1983. 90-day vapor inhalation toxicity study of hydrogen sulfide in Fischer 344 rats. CIIT Docket No 22063. Chemical Industry Institute of Toxicology, ResearchTriangle Park, NC.	Decreased body weight

REPEAT DOSE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LOAEL/ Duration**	**Reference**	**Comments**
Carbon Monoxide	630-08-0	Inhalation	Monkey	≤100 ppm/ 24 wk	DeBias DA, Banerjee, CM, Birkhead, NC, Harrer, WV and LA Kazal. 1973. Effects of carbon monoxide inhalation on ventricular fibrillation. Arch Environ Health 27: 161-167.	Reduced threshold for ventricular defribrillation. Study helps support derivation of AEGL-2 which is based on human data.

***IN VITRO* GENETIC TOXICITY**					
Component	**CAS No.**	**Assay**	**Results**	**Reference**	**Comments**
C1-C4	Various; see Appendix 4	All non mammalian and mammalian systems tested	Negative	See Appendix 4.	
C5-C6	Several; see gasoline blending streams Category Analysis Document, 2008	Non-mammalian Mammalian	Negative Negative	API (American Petroleum Institute) 1977a. Mutagenicity evaluation of unleaded gasoline (L5178Y Mouse lymphoma assay and Ames test) API Rpt #28-30173 Washington, DC. [report includes single ip dose *in vivo* cytogenetic assay].	
Nitrogen	7727-37-9	No specific data; considered a simple asphyxiant		McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.
Hydrogen	1333-74-0	No specific data; considered a simple asphyxiant		McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.

***IN VITRO* GENETIC TOXICITY**					
Component	**CAS No.**	**Assay**	**Results**	**Reference**	**Comments**
Carbon Dioxide	124-38-9	No specific data; considered a simple asphyxiant		McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.
1,3-Butadiene	106-99-0	Non-mammalian Mammalian	Positive Weakly positive	Arce, GT, Vincent, DR, Cunningham, MJ Choy, WN and AM Sarrif. 1990. *In vitro* and *in vivo* genotoxicity of 1,3-butadiene and metabolites. Environ. Health Perspect. 86:75-8. Sasiadek, M, Järventaus, H and M Sorsa. 1991. Sister-chromatid exchanges induced by 1,3-butadiene and its epoxides in CHO cells. *Mutat Res*. **263;** 47-50.	Several studies conducted; In general, the mammalian studies were poorly reported or had flaws, but consensus appears that material is weakly positive with metabolic activation. Representative studies used for robust summary.
Benzene	71-43-2	Non-mammalian Mammalian	Many negative, but one positive Positive	Glatt, H, Padykula, R, Berchtold, GA, Ludwig, G, Platt, KL, Klein, J and F Oesch. 1989. Multiple activation pathways of benzene leading to products with varying genotoxic characteristics. Environ Health Perspect 82:81-89. Morimoto K. 1983. Induction of sister chromatid exchanges and cell division delays in human lymphocytes by microsomal activation of benzene. Cancer Res 43:1330-1334.	Multiple studies; Representative positive studies used for robust summary.

***IN VITRO* GENETIC TOXICITY**					
Component	**CAS No.**	**Assay**	**Results**	**Reference**	**Comments**
Methyl Mercaptan	74-93-1	Non-mammalian Mammalian	Negative Negative	ELF Atochem. 1992. Sodium methyl mercaptide. Reverse mutation assay by the Amestest. CIT Report no. 9102 MO, 7 August 1992 ELF Atochem. 1995. In vitro mammalian chromosome aberration test in cultured human lymphocytes with sodium methylmercaptide. CIT report no. 12086 MLH, 15 November 1995.	Material tested - Methanethiol, sodium salt (5188-07-8) Sodium Methylmercaptide
Ethyl Mercaptan	75-08-01	Non-mammalian Mammalian	Negative Positive	Hazleton Laboratories, Inc. 1984. Salmonella typhimurium mammalian microsome plate incorporation assay with ethyl mercaptan, May 5, 1983. Project No. 652-145. Hazleton Laboratories, Inc. 1984. *In vitro* Sister Chromatid Exchange in Chinese hamster ovary cells. Ethyl Mercaptan. Final Report. December 11, 1984. OTS0571888.	The AEGL document on ethyl mercaptan indicates that the limited genotoxicity data are equivocal. (only one dose level, in the absence of metabolic activation, elicited a two-fold response)..
Ammonia	7664-41-7	Non-mammalian	Negative	Shimizu H, Suzuki, Y, Takemura, N, Goto, S and H Matsushita. 1985. The results of microbial mutation test for forty-three industrial chemicals, Jap J Ind Health 27, 400-419.	In addition, studies on ammonium salts have been generally negative
Hydrogen Sulfide	7783-06-4	Non-mammalian	Negative	Hughes, T, Sparacino, C and S Frazier. 1984. Validation of chemical and biological techniques for evaluation of vapors in ambient air/mutagenicity testing of twelve (12) vapor-phase compounds. Research Triangle Park, NC: U.S. Environmental Protection Agency, Health Effects Research Laboratory. EPA/600/1-84/005. (NTIS PB84164219).	Study limited by solubility of H2S in test system.

***IN VITRO* GENETIC TOXICITY**					
Component	**CAS No.**	**Assay**	**Results**	**Reference**	**Comments**
Carbon Monoxide	630-08-0	Non-mammalian	Negative	Doolittle, DJ, Rahn, CS, and DK Lee. 1991. The effect of exposure to nicotine, carbon monoxide, cigarette smoke or cigarette smoke condensate on the mutagenicity of rat urine. Mutat Res, 260: 9-18.	Study limited by lack of sensitivity in detecting mutagenic components in urine following inhalation exposure.

***IN VIVO* GENETIC TOXICITY**					
Component	**CAS No.**	**Assay**	**Results**	**Reference**	**Comments**
C1-C4	Various; see Appendix 4	All non mammalian and mammalian systems tested	Negative	See Appendix 4.	
C5-C6	Several; see gasoline blending streams Category Analysis Document, 2008	Micronuclei formation, rats	Negative	API (American Petroleum Institute) 2005b. Baseline Gasoline Vapor Condensate. Micronucleus Assay in a 13 week Whole Body Inhalation Toxicity Study in Rats with Neurotoxicity Assessments and 4-week In Vivo Genotoxicity and Immunotoxicity Assessments. HLS Study No. 00-6125, Vol IV, Appendix X. Huntingdon Life Sciences Laboratories, East Millstone, NJ and Huntingdon Eye Research Center, Suffolk, UK. API (American Petroleum Institute) 2005c. Baseline Gasoline Vapor Condensate. Sister Chromatid Exchange Assay in a 13 week Whole Body Inhalation Toxicity Study in Rats with Neurotoxicity Assessments and 4-week In Vivo Genotoxicity and Immunotoxicity Assessments. HLS Study No. 00-6125, Vo. IV, Appendix Y. Huntingdon Life Sciences Laboratories, East Millstone, NJ and BioReliance Laboratories, Rockville, MD.	

***IN VIVO* GENETIC TOXICITY**					
Component	**CAS No.**	**Assay**	**Results**	**Reference**	**Comments**
Nitrogen	7727-37-9	No specific data; considered a simple asphyxiant		McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.
Hydrogen	1333-74-0	No specific data; considered a simple asphyxiant		McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.
Carbon Dioxide	124-38-9	No specific data; considered a simple asphyxiant		McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.

***IN VIVO* GENETIC TOXICITY**					
Component	**CAS No.**	**Assay**	**Results**	**Reference**	**Comments**
1,3-Butadiene	106-99-0	Micronuclei formation, mice	Positive	Autio, K, Renzi, L, Catalan, J, Albrecht, OE, and M Sorsa. 1994. Induction of micronuclei in peripheral blood and bone marrow erythrocytes of rats and mce exposed to 1,3-butadiene by inhalation. Mut. Res. 309:315-320.	Inhalation, mice, 500 ppm = maximum concentration tested. KS=1. Studies conducted on crude butadiene streams were also positive. Same study was negative in rats.
Benzene	71-43-2	Sister chromatid exchange and blood micronuclei formation, mice	Positive	Erexson, GL, Wilmer, JL, Steinhagen, WH, and AD Kilgerman. 1986. Induction of Cytogenetic Damage in Rodents after Short-Term Inhalation of Benzene. Environ. Mutagen. 8:29-40.	Multiple studies; Study reported lowest concentration of benzene (1 ppm for SCE and 3 ppm for micronuclei formation) to induce genotoxicity.
Methyl Mercaptan	74-93-1	Micronuclei formation, mice	Negative	Elf Atochem North America. 1997. Bone marrow micronucleus assay in male and female Swiss-Webster mice following acute nose-only inhalation exposure to methyl mercaptan. SRI International report no. M020-95, 8 January 1997.	512 ppm = maximum concentration tested.
Ethyl Mercaptan	75-08-01	No data; read across from methyl methyl mercaptan			
Ammonia	7664-41-7	Micronuclei formation, mice	Negative	Hayashi ,M, Kishi, M, Sofuni, T and M Ishidate Jr. 1988. Micronucleus test in mice on 39 food additives and eight miscellaneous chemicals. Food. Chem.Toxicol. 26, 487-500. Studies summarized in: World Health Organization (WHO). 1986. Ammonia – Environmental Health Criteria 54. Geneva: International Programme on Chemical Safety. Clement Associates, Inc. 1990. Health Effects Assessment for	Ammonium chloride and ammonium sulfate General conclusion is that there are no data to show that ammonia is mutagenic in mammals.

***IN VIVO* GENETIC TOXICITY**					
Component	**CAS No.**	**Assay**	**Results**	**Reference**	**Comments**
				Ammonia. Prepared for The Fertilizer Institute, Washington, D.C. BIBRA. 1995. Toxicology Profile: Ammonia. BIBRA International.	
Hydrogen Sulfide	7783-06-4	No data; read across from methyl mercaptan	Negative		
Carbon Monoxide	630-08-0	No data			

REPRODUCTIVE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LOAEL**	**Reference**	**Comments**
C1-C4 (Isobutane has lowest LOAEL for this group of consituents)	75-28-5	Inhalation	Rat	9000 ppm	HLS (Huntinton Life Sciences), 2008. Isobutane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4244.	Post-implantation loss observed
C5-C6	Several; see gasoline blending streams Category Analysis Document, 2008	Inhalation	Rat	NOAEL $\geq$ 6521 ppm (highest dose tested)	API (American Petroleum Institute) 2008c Baseline Gasoline Vapor Condensate, A 2-Generation Whole Body Inhalation Reproductive Study in Rats. HLS Study No. 00-4207. Huntingdon Life Sciences Laboratories, East Millstone, NJ.	
Nitrogen	7727-37-9	No specific data; considered a simple asphyxiant			McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.

REPRODUCTIVE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LOAEL**	**Reference**	**Comments**
Hydrogen	1333-74-0	No specific data; considered a simple asphyxiant			McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.
Carbon Dioxide	124-38-9	No specific data; considered a simple asphyxiant			McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.

REPRODUCTIVE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LOAEL**	**Reference**	**Comments**
1,3-Butadiene	106-99-0	Inhalation	Rat	NOAEL ≥ 6000 ppm) (highest dose tested)	WIL Research Laboratories. 2003. An inhalation reproduction/developmental toxicity screening study of 1,3-butadiene in rats (unpublished report). (WIL-186024). WIL Research Laboratories, Inc., Ashland, OH, USA.	
Benzene	71-43-2	Inhalation	Mice	300ppm/ 13 wk	Ward, CO, Kuna, RA, Snyder, NK Alsaker, RD, Coate, WB, and PH Craig. 1985. Subchronic inhalation toxicity of benzene in rats and mice. Americ. Journ. of Industrial Medicine 7: 457-473.	Reproductive organ and sperm effects.
Methyl Mercaptan	74-93-1	No Data – read across from H2S				
Ethyl Mercaptan	75-08-01	No Data – read across from H2S				
Ammonia	7664-41-7	Inhalation	Pig	NOAEL ≥ 35 ppm (highest dose tested)	Diekman, MA., Scheidt, AB., Sutton, AL., Green, ML., Clapper, JA, Kelly, DT., and WG Van Alstine, 1993. Growth and reproductive performance, during exposure to ammonia, of gilts afflicted with pneumonia and atrophic rhinitis. Am J Vet Res 54(12):2128-2131.	Pig study not considered adequate to assess reproductive toxicity of ammonia. However, a well-conducted feeding study in rats on diammonium phosphate resulted in no effects on reproduction or development. Another well-conducted repeat dose study in rats on ammonium sulfate also did not result in effects on the reproductive organs.

REPRODUCTIVE TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LOAEL**	**Reference**	**Comments**
Hydrogen Sulfide	7783-06-4	Inhalation	Rat	NOAEL ≥80 ppm (highest dose tested)	Dorman, DC, Struve, MF, Gross, EA and KA Brenneman. 2000. Fertility and developmental neurotoxicity effects of inhaled hydrogen sulfide in Sprague-Dawley rats. Neurotoxicology and Teratology. 22:71-84.	
Carbon Monoxide	630-08-0	Inhalation	Rat	≤30 ppm	Garvey, DJ and LD Longo. 1979. Chronic low level maternal carbon monoxide exposure and fetal growth and development. BioI. Reprod. 19:8-14.	Reduced fertility/implantation

DEVELOPMENTAL TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LOAEL**	**Reference**	**Comments**
C1-C4 (2-butene has lowest NOAEL for this group of consituents)	107-07-7	Inhalation	Rat	NOAEL ≥ 5000 ppm (highest dose tested)	Waalkens-Brendsen, DHand JHE Arts.1992. Combined short term inhalation and reproductive/developmental toxicity screening test with butene-2 in rats. Proj. #B91-8336 (Study #1410) [2-butene].	
C5-C6	Several; see gasoline blending streams Category Analysis Document, 2008	Inhalation	Rat	463 ppm	API (American Petroleum Institute) 2009. Baseline Gasoline Vapor Condensate. Whole-Body Inhalation Developmental Toxicity Study in Mice with Baseline Gasoline Vapor Condensate. EMBSL #MRD-00-695:169534M. ExxonMobil Biomedical Sciences Inc., Annandale, NJ.	Rat study with same test material, protocol and doses was negative.
Nitrogen	7727-37-9	No specific data; considered a simple asphyxiant			McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.

DEVELOPMENTAL TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LOAEL**	**Reference**	**Comments**
Hydrogen	1333-74-0	No specific data; considered a simple asphyxiant			McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.
Carbon Dioxide	124-38-9	No specific data; considered a simple asphyxiant			McManus, N. 1999. *Safety and Health in Confined Spaces*. Lewis Publishers, Boca Raton, FL. NIOSH. 1980 U.s. National Institute for Occupational Safety and Health: Working in Confined Spaces. DHHS (NIOSH) Pub. No. 80-106. NIOSH, Cincinnati, OH. NIOSH. 1987 U.s. National Institute for Occupational Safety and Health: NIOSH Respirator Decision Logis. DHHS (NIOSH) Pub. No. 87-108. NIOSH, Cincinnati, OH.	Standard secondary source information.
1,3-Butadiene	106-99-0	Inhalation	Rat	NOAEL≥1000 ppm (highest dose tested)	Morrissey, R, Schwetz, B, Hackett, P, Sikov, M, Hardin, B, McClanahan, B, Decker, J and T Mast. 1990. Overview of reproductive and developmental toxicity studies of 1,3-butadiene in rodents. Environ. Health Perspect. **86**, 79-84.	OECD 414 Study

DEVELOPMENTAL TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LOAEL**	**Reference**	**Comments**
Benzene	71-43-2	Inhalation	Mice	20ppm	Keller, KA, and CA Snyder. 1986. Mice exposed in utero to low concentrations of benzene exhibit enduring changes in their colony forming hematopoietic cells. Toxicology 42: 171-181. Keller, KA and CA Snyder. 1988. Mice exposed in utero to 20 ppm benzene exhibit altered numbers of recognizable hematopoietic cells up to seven weeks after exposure. Fundam. Appl. Toxicol. 10: 224-232.	Hematological effect in neonates and 6 week old offspring.
Methyl Mercaptan	74-93-1	No Data – read across from H2S				
Ethyl Mercaptan	75-08-01	No Data; read across from H2S				
Ammonia	7664-41-7	Inhalation	pig	NOAEL ≥35 ppm (highest dose tested)	Diekman, MA, Scheidt, AB, Sutton, AL, Green, ML, Clapper, JA, Kelly, DT, and WG Van Alstine. 1993. Growth and reproductive performance, during exposure to ammonia, of gilts afflicted with pneumonia and atrophic rhinitis. Am J Vet Res 54(12):2128-2131.	Pig study not considered adequate to assess reproductive toxicity of ammonia. However, a well-conducted feeding study in rats on diammonium phosphate resulted in no effects on reproduction or development.
Hydrogen Sulfide	7783-06-4	Inhalation	Rat	NOAEL ≥ 80 ppm (highest dose tested)	Dorman, DC, Struve, MF Gross, EA and KA Brenneman. 2000. Fertility and developmental neurotoxicity effects of inhaled hydrogen sulfide in Sprague-Dawley rats. Neurotoxicology and Teratology. 22:71-84.	

DEVELOPMENTAL TOXICITY						
Component	**CAS No.**	**Route**	**Species**	**LOAEL**	**Reference**	**Comments**
Carbon Monoxide	630-08-0	Inhalation	Mice	65 ppm	Singh J and LH Scott. 1984. Threshold for carbon monoxide induced fetotoxicity. Teratology 30: 253-257. Singh J. 1986. Early Behavioral Alterations in Mice Follwing Prenatal Carbon Monoxide Exposure. NeuroToxicology 7: 475-482.	Postnatal neurobehavioral development at day 14. .

Appendix 4

Literature Evaluated for Selection of C1-C4 Key Studies[2]

ACUTE TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Acute Inhalation/LC50 (simple asphyxiant)	Methane	74-82-8	ACGIH Documentation of. TLV's on simple asphyxiants		Standard secondary source info
Acute Aquatic LC50 and EC50				ECOSAR model in EPI-Suite™ (EPA, 2000)	
Acute Inhalation/LC50 (simple asphyxiant)	Ethane	74-84-0	ACGIH Documentation of. TLV's on simple asphyxiants		Standard secondary source info
Acute Aquatic LC50 and EC50				ECOSAR model in EPI-Suite™ (EPA, 2000)	
Acute Inhalation/LC50 (rat, >800,000 ppm,15 min)	n-Propane	74-98-6	API HPV Robust Summary & Test Plan – Petroleum Gases	Clark, DG and D.J Tinson. 1982. acute inhalation toxicity of some halogenated and non-halogenated hydrocarbons. Human Toxicol. Vol. 1, pp 239-247.	KS=2
Acute Aquatic LC50 and EC50				ECOSAR model in EPI-Suite™ (EPA, 2000)	
Acute Inhalation/LC50 (rat, 276,000 ppm, 4 hr)	n-Butane	106-97-8	API HPV Robust Summary & Test Plan – Petroleum	Shugaev, BB. 1969. Concentrations of	Not considered valid in HPV plan, but used in

[2] Highlighted text indicates key study selected.

ACUTE TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
			Gases	hydrocarbons in tissues as a measure of toxicity. Arch. Environ. Health 18:878882.	other SIDS document.
Acute Aquatic LC50 and EC50				ECOSAR model in EPI-Suite™ (EPA, 2000)	
Acute Inhalation/LC50 (rat, 520,400 ppm, 2 hr)	Isobutane	75-28-5	API HPV Robust Summary & Test Plan – Petroleum Gases	Aviado, DM, Zakhari, S and Wanatabe, T. 1977. Isobutane, Chapter 6 pp 61-72 in Non-Fluorinated propellants and solvents for aerosols. CRC Press, Cleveland, Ohio.	KS=2
Acute Aquatic LC50 and EC50				ECOSAR model in EPI-Suite™ (EPA, 2000)	
Acute Inhalation/LC50 (simple asphyxiant)	LPG	Mixture; mostly propane	ACGIH Documentation of. TLV's on simple asphyxiants		Standard secondary source info
Acute Inhalation/LC50 (rat, >950,000 ppm, 4 hr)	Ethylene	74-85-1	SIAR, Ethylene	Flury, F. 1928. Arch Exp Pathol Pharmacol.138:65.	
Acute Inhalation/LC50 (rat, >65,000 ppm, 4 hr)	Propylene	115-07-1	SIAP, Propylene/ Robust Summaries for Propylene Category, ACC Olefins Panel.	Conolly R and T Osimitz. 1981. Biochemical aspects of propylene hepatotoxicity. Toxicologist l, 112 (Abstract 406).	Low order of toxicity-narcosis induced in humans at 46,000 ppm and lower flammability limit is 20,000 ppm.
Acute Inhalation/LC50 (rat, LC50 >10,000 ppm, 4 hr)	2-Butene	107-07-7	SIAP, Butenes/ Robust Summaries for Low 1,3-Butadiene C4 Category,	Arts, JHE. 1992. Acute (4-hour) inhalation toxicity study of	OECD limit test

ACUTE TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
			ACC Olefins panel.	butene-2 in rats. Report No. V92.183/352130. TNO Nutrition and Food Research, Zeist, The Netherlands. [2butene]	
Acute Inhalation/LC50 (rat, 270,000 ppm, 4 hr)	Isobutylene	115-11-7	SIAR, Isobutylene/ Robust Summaries for Low 1,3-Butadiene C4 Category, ACC Olefins panel.	Shugaev, BB. 1969. Concentrations of hydrocarbons in tissues as a measure of toxicity. Arch. Environ. Health 18:878882.	Low order of toxicity – nacrosis induced in humans at >18,000 ppm, the LEL.
Acute Inhalation/LC50 (rat, >900,000 ppm, 2 hr); Considered a simple asphyxiant	Acetylene	74-86-2	HPV Test Plan – Acetylene, ACC , 2005	Riggs LK. 1925. The physiologic properties of some unsaturated hydrocarbons. Proc Soc Exp Biol Med 22: 269-270	LC50 in humans determined to be >100,000 ppm, which was considered critical SIDS study in test plan.

REPEAT DOSE TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Repeated Dose (simple asphyxiant)	Methane	74-82-8	ACGIH Documentation of TLVs		Standard secondary information
Repeated Dose Inhalation/ 28 day (NOAEL ≥16,000 ppm)	Ethane	74-84-0	API HPV Robust Summary & Test Plan – Petroleum Gases	HLS (Huntinton Life Sciences), 2008. Ethane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4243.	KS=1; OECD 422
Repeated Dose Inhalation/ 28 day (Rat, NOAEL ≥4,000 ppm)	n-Propane	74-98-6	API HPV Robust Summary & Test Plan – Petroleum Gases	HLS (Huntinton Life Sciences), 2008. n-Propane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4245.	KS=1; OECD 422

REPEAT DOSE TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Repeated Dose Inhalation/ 28 day (Rat, NOAEL ≥9,000 ppm)	n-Butane	106-97-8	API HPV Robust Summary & Test Plan – Petroleum Gases	HLS (Huntinton Life Sciences), 2008. n-Butane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4242.	KS=1; OECD 422
Repeated Dose Inhalation/ 28 day (Rat, NOAEL ≥9,000 ppm)	Isobutane	75-28-5	API HPV Robust Summary & Test Plan – Petroleum Gases	HLS (Huntinton Life Sciences), 2008. Isobutane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4244.	KS=1; OECD 422
Repeated Dose Inhalation/ 13 wk (Rat, NOAEL ≥10,000 ppm)	LPG	Mixture; mostly propane		HLS (Huntinton Life Sciences), 2008. LPG: 13-Week whole body inhalation toxicity study in rats with neurotoxicity assessments and *in vivo* genotoxicity assessments. Conducted for the American Petroleum Insitute. Draft report 03-6141.	KS=1; OECD 413/474

REPEAT DOSE TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Repeated Dose Inhalation/ 90 day (NOAEL ≥ 10,000 ppm)	Ethylene	74-85-1	SIAR, Ethylene	Chemical Industry Institute of Toxicology, Research Triangle Park, North Carolina, USA. CIIT summary report, a ninety day inhalation toxicology study in albino rats exposed to atmospheric ethylene gas. 1977.	
Repeated Dose Inhalation/ 103 wk (rat, NOAEL ≥ 5,000 ppm)	Propylene	115-07-1	SIAP, Propylene; Robust Summaries for Propylene Streams, ACC	National Toxicology Program. 1985. Toxicology and carcinogenesis studies of propylene (CAS No. 115-07-1) in F344/N rats and B6C3F1 mice (inhalation studies). Report NTP TR 272, National Toxicology Program, U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health. Research Triangle Park, NC, USA.	Inflammation of nasal cavity seen at 5000 ppm, but study considered negative.
Repeated Dose Inhalation/ 39-46 d (rat, LOAEL== 5,000 ppm; NOAEL = 2500 ppm)	2-Butene	107-07-7	SIAP, Butenes/ Robust Summaries for Low 1,3-Butadiene C4 Category, ACC Olefins panel.	Waalkens-Brendsen, DH and JHE Arts. 1992. Combined short term inhalation and reproductive/developmental toxicity screening test with Butene-2 in rats. Proj. #B91-8336 (Study #1410) [2-butene]	KS=1. Body weight reduced. Repeat dose NOAEL for 1-butene = 8000 ppm.

REPEAT DOSE TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Repeated Dose Inhalation/ 105 wk (rat, LOAEL=8,000; NOAEL = 2000 ppm)	Isobutylene	115-11-7	SIAR, Isobutylene/ Robust Summaries for Low 1,3-Butadiene C4 Category, ACC Olefins panel.	National Toxicology Program (NTP). 1998. Toxicology and carcinogenesis studies of isobutene (CAS No. 115-11-7) in F344/N Rats and B6C3F1 Mice (inhalation studies). Report NTP TR 487, National Toxicology Program, U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health. Research Triangle Park, NC, USA.	Considered a critical SIDS endpoint study in OECD document
Repeated Dose Inhalation/ 6 mo (rat & dog , LOAEL≤28,700 ppm)	Acetylene	74-86-2	HPV Test Plan – Acetylene, ACC , 2005	Horn HJ, Weir RJ Jr and Reese WH. 1957. Inhalation toxicology of methylacetylene. Arch Ind Health 15: 20-26.	KS=2. Analog methyl-acetylene study. Only one concentration studied, but was considered to be valid with restrictions

***IN VITRO* GENETIC TOXICITY**					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Genetic Tox – *In Vitro* Nonmammalian system – *salmonella typhimurium* (negative)	Methane	74-82-8		National Toxicology Program (NTP). 1993. Salmonella test on methane. NTP Report 297396. National Toxicology Program, U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health. Research Triangle Park, NC, USA.	
No data	Ethane	74-84-0			
Genetic Tox – *In Vitro* Nonmammalian system – *salmonella typhimurium* (negative)	n-Propane	74-98-6	API HPV Robust Summary & Test Plan – Petroleum Gases	Kirwin, CJ and Thomas, WC. 1980. In vitro microbio-logical mutagenicity studies of hydro-carbon propellants. J. Soc. Cosmet. Chem. Vol. 31.) pp 367-370	KS=2
Genetic Tox – *In Vitro* Nonmammalian system – *salmonella typhimurium* (negative)	n-Butane	106-97-8	API HPV Robust Summary & Test Plan – Petroleum Gases	Kirwin, CJ and Thomas, WC. 1980. In vitro microbio-logical mutagenicity studies of hydro-carbon propellants. J. Soc. Cosmet. Chem. Vol. 31.) pp 367-370	KS=2
Genetic Tox – *In Vitro* Nonmammalian system – *salmonella typhimurium* (negative)	Isobutane	75-28-5	API HPV Robust Summary & Test Plan – Petroleum Gases	Kirwin, CJ and Thomas, WC. 1980. In vitro microbio-logical mutagenicity studies of hydro-carbon propellants. J. Soc. Cosmet. Chem. Vol. 31.) pp 367-370	KS=2

***IN VITRO* GENETIC TOXICITY**					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
No data	LPG	Mixture; mostly propane			
Genetic Tox – *In Vitro* Nonmammalian system – *salmonella typhimurium* (negative) Genetic Tox – *In Vitro* Mammalian system – CHO chromosomal aberrations (negative)	Ethylene	74-85-1	SIAR, Ethylene	Hamm TE jr, Guest D, Dent JG. Chronic toxicity and oncogenicity bioassay of inhaled ethylene in Fisher-344 rats. Fundamental and Appl Toxicol. 1984;4:473-8. Riley S. Ethylene: Induction of chromosome aberrations in cultured chinese hamster ovary (CHO) cells. Corning Hazleton Report No. 1458/1-1052, April 1996.	
Genetic Tox – *In Vitro* Nonmammalian system – *salmonella typhimurium* (negative) Genetic Tox – *In Vitro* Mammalian system – mouse lymphoma (negative)	Propylene	115-07-1	SIAP, Propylene	Inveresk. 2003. Ames test draft report. Inveresk Research. McGregor, D, Brown, AG, Cattanack, P, Edwards, I, McBride, D, Riach, C, Shepherd, W and WJ Caspary. 1991. Responses of the L5178Y mouse lymphoma forward mutation assay: V. Gases and vapors. Environ. Mol. Mutag., 17:122-129.	Positive in single bacterial strain in Ames assay in presence of s9, but negative in other strains.

***IN VITRO* GENETIC TOXICITY**					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Genetic Tox – *In Vitro* Nonmammalian system – *salmonella typhimurium* (negative) Genetic Tox – *In Vitro* Mammalian system – rat lymphocyte clastogenicity (negative)	2-Butene	107-07-7	SIAP, Butenes/ Robust Summaries for Low 1,3-Butadiene C4 Category, ACC Olefins panel.	Thompson, PW. 1992. Butene-2: Reverse mutation assay "Ames test" using *Salmonella typhimurium*. Proj. #44/812. SafePharm Laboratories, UK, Derby UK. [2-butene] Wright, NP. 1992. Butene-2: Metaphase analysis in rat lymphocytes *in vitro*. Proj. #44/813. SafePharm Laboratories, UK, Derby UK. [2-butene]	1-butene and isobutylene also negative. Isobutylene also negative

***IN VITRO* GENETIC TOXICITY**					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Genetic Tox – *In Vitro* Nonmammalian system – *salmonella typhimurium* (negative) Mammalian system – mouse embryo fibroblast transformations; mouse lymphoma (negative)	Isobutylene	115-11-7	SIAR, Isobutylene/ Robust Summaries for Low 1,3-Butadiene C4 Category, ACC Olefins panel.	McGregor, DB, Reach, CG. 1981. Isobutylene: Ames test for mutagenic activity with salmonella TA 1535, TA100, TA1537, TA1538, TA98, and e.coli WP2 uvrB) pKM101), unpublished rpt# 2098, IRI Proj. 704338 Inveresk Research Institute, for Essochem Europe, Inc. Machelen, Belgium McGregor, DB, Poole, A. 1981. Isobutylene: induction of morphological transformation in C3H/10T½ clone 8 cells. Inveresk Research International, Musselburgh, Scotland for Essochem Europe, Inc., Machelen, Belgium McGregor, D.B., Ross, C.A. 1981. Isobutylene: assessment of mutagenic potential in the mouse lymphoma mutation assay. Inveresk Research International, Musselburgh, Scotland for Essochem Europe Inc., Machelen, Belgium.	

***IN VITRO* GENETIC TOXICITY**					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Genetic Tox – *In Vitro* Nonmammalian system – *salmonella typhimurium* (negative)	Acetylene	74-86-2	HPV Test Plan – Acetylene, ACC, 2005	Hughes TJ, Sparacino, C and S Frazier. 1984. Validation of chemical and biological techniques for evaluation of vapors in ambient air/mutagenicity testing of twelve (12) vapor-phase compounds. EPA Report Number 68-02-3170, NTIS Publication PB84-164219.	Also applies to methacetylene; methacetylene was positive in *e.coli* assay, but general weight of evidence for acetylene judged to be negative

IN VIVO GENETIC TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
No data	Methane	74-82-8			
No data	Ethane	74-84-0			
No data	n-Propane	74-98-6			
No data	n-Butane	106-97-8			
No data	Isobutane	75-28-5			
Genetic Tox – *In Vivo* Micronuclei formation (negative)	LPG	Mixture; mostly propane		HLS (Huntinton Life Sciences), 2008. LPG: 13-Week whole body inhalation toxicity study in rats with neurotoxicity assessments and *in vivo* genotoxicity assessments. Conducted for the American Petroleum Insitute. Draft report 03-6141.	KS=1; Rat; OECD 413/474
Genetic Tox – *In Vivo* Bone marrow /blood micronuclei formation (negative)	Ethylene	74-85-1	SIAR, Ethylene	Vergenes, JS and IM Pritts. 1994. Effects of ethylene on micronucleus formation in the bone marrow of rats and mice following four weeks of inhalation exposure. Mutat Res.324: 87-91.	Mouse, inhalation, 3,000 ppm maximum concentration tested
Bone marrow /blood micronuclei formation (negative)	Propylene	115-07-1	SIAP, Propylene	DuPont (2002). Propylene biomarker/mutagenicity dose-response study in rats. Rat bone marrow micro-nucleus assay by inhalation. DuPont Haskell Laboratory. Report No. DuPont-9106.	Mouse, inhalation, 10,000 ppm maximum concentration tested

IN VIVO GENETIC TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Bone marrow /blood micronuclei formation (negative)	1-Butene	106-98-9	SIAP, Butenes/ Robust Summaries for Low 1,3-Butadiene C4 Category, ACC Olefins panel.	Khan, SH, and CO Ward. 1985. Micronucleus test of Gulftene® 4. Unpublished report # 84-2113 by Gulf Life Sciences Center for Gulf Oil Chemicals Co. [1-butene]	Mouse, inhalation, 22,000 ppm maximum concentration tested; 1-butene; also see isobutylene results
Bone marrow /blood micronuclei formation (negative)	Isobutylene	115-11-7	SIAR, Isobutylene/ Robust Summaries for Low 1,3-Butadiene C4 Category, ACC Olefins panel.	Przygoda, R. 1990. *In vivo* mammalian bone marrow micronucleus assay for isobutylene. Project #236030. Exxon Biomedical Sciences Inc. East Millstone, NJ	Mouse, inhalation, 10,000 ppm maximum concentration tested
Genetox in vivo (to be determined)	Acetylene	74-86-2	HPV Test Plan – Acetylene, ACC , 2005	To be determined per test plan.	

REPRODUCTIVE TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
No data	Methane	74-82-8			
Reproductive Tox Inhalation (Rat, NOAEL ≥16,000 ppm)	Ethane	74-84-0	API HPV Robust Summary & Test Plan – Petroleum Gases	HLS (Huntinton Life Sciences), 2008. Ethane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4243.	KS=1; OECD 422
Reproductive Tox Inhalation (Rat, NOAEL ≥12,000 ppm)	n-Propane	74-98-6	API HPV Robust Summary & Test Plan – Petroleum Gases	HLS (Huntinton Life Sciences), 2008. n-Propane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4245.	KS=1; OECD 422
Reproductive Tox Inhalation (Rat, NOAEL ≥9,000 ppm)	n-Butane	106-97-8	API HPV Robust Summary & Test Plan – Petroleum Gases	HLS (Huntinton Life Sciences), 2008. n-Butane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4242.	KS=1; OECD 422

REPRODUCTIVE TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Reproductive Tox Inhalation (Rat, LOAEL =9,000 ppm; NOAEL = 3,000)	Isobutane	75-28-5	API HPV Robust Summary & Test Plan – Petroleum Gases	HLS (Huntinton Life Sciences), 2008. Isobutane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4244.	KS=1; OECD 422; Post-implantation loss observed
Reproductive Tox Inhalation (Rat, NOAEL ≥10,000 ppm)	LPG	Mixture; mostly propane	API HPV Robust Summary & Test Plan – Petroleum Gases	HLS (Huntinton Life Sciences), 2008. LPG: 13-Week whole body inhalation toxicity study in rats with neurotoxicity assessments and *in vivo* genotoxicity assessments. Conducted for the American Petroleum Insitute. Draft report 03-6141.	KS=1 (OECD 413/474 study) Sperm morphology study also included in protocol
Reproductive Tox Inhalation (Rat, NOAEL ≥5,000 ppm)	Ethylene	74-85-1	SIAR, Ethylene	Aveyard L. 1996. Ethylene: Inhalation (Head-only) Reproduction/Development Toxicity Study in the Rat. Corning Hazleton Report No. 1458/2-1050.	

REPRODUCTIVE TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
No data	Propylene	115-07-1			No effects observed on reproductive organs in two species during NTP repeat dose studies of 14 or 103 wk.
Reproductive Tox Inhalation (Rat, NOAEL ≥5,000 ppm)	2-butene	107-07-7	SIAP, Butenes/ Robust Summaries for Low 1,3-Butadiene C4 Category, ACC Olefins panel.	Waalkens-Brendsen, DH and JHE Arts. 1992. Combined short term inhalation and reproductive/developmental toxicity screening test with Butene-2 in rats. Proj. #B91-8336 (Study #1410) [2-butene]	
No data	Isobutylene	115-11-7			No effects observed on reproductive organs in two species during repeat dose study.
No data – see comments	Acetylene	74-86-2	HPV Test Plan – Acetylene, ACC , 2005		HPV Test Plan indicates that reproductive and developmental toxicity of acetylene is unlikely, therefore no testing has been scheduled.

DEVELOPMENTAL TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
No data	Methane	74-82-8			
Developmental Tox Inhalation (Rat, NOAEL ≥16,000 ppm)	Ethane	74-84-0	API HPV Robust Summary & Test Plan – Petroleum Gases	HLS (Huntinton Life Sciences), 2008. Ethane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4243.	KS=1; OECD 422
Developmental Tox Inhalation (Rat, NOAEL ≥12,000 ppm)	n-Propane	74-98-6	API HPV Robust Summary & Test Plan – Petroleum Gases	HLS (Huntinton Life Sciences), 2008. n-Propane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4245.	KS=1; OECD 422
Developmental Tox Inhalation (Rat, NOAEL ≥9,000 ppm)	n-Butane	106-97-8	API HPV Robust Summary & Test Plan – Petroleum Gases	HLS (Huntinton Life Sciences), 2008. n-Butane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4242.	KS=1; OECD 422

DEVELOPMENTAL TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Developmental Tox Inhalation (Rat, NOAEL ≥9,000 ppm)	Isobutane	75-28-5	API HPV Robust Summary & Test Plan – Petroleum Gases	HLS (Huntinton Life Sciences), 2008. Isobutane: Combined repeated exposure toxicity, reproduction and neurotoxicity screening in rats via whole-body inhalation exposures. Conducted for the American Petroleum Insitute. Draft report 03-4244.	KS=1; OECD 422;
Developmental Tox Inhalation (Rat, NOAEL ≥10,000 ppm)	LPG	Mixture; mostly propane		HLS (Huntinton Life Sciences), 2008. LPG: Embryo-fetal toxicity study in rats by inhalation exposure.. Conducted for the American Petroleum Insitute. Draft report 03-42-53.	KS=1 (OECD 414)
Developmental Tox Inhalation (Rat, NOAEL ≥10,000 ppm)	Ethylene	74-85-1	SIAR, Ethylene	Aveyard L. 1996. Ethylene: Inhalation (Head-only) Reproduction/Development Toxicity Study in the Rat. Corning Hazleton Report No. 1458/2-1050.	
Developmental Tox Inhalation (Rat, NOAEL ≥10,000 ppm)	Propylene	115-07-1	SIAP, Propylene	BASF Aktiengesellschaft 2002. Propylene - Prenatal developmental inhalation toxicity study in Wistar rats; vapor exposure. Experimental Toxicology and Ecology Laboratory, Rhein, Germany. Project #31R0416/01019.	

DEVELOPMENTAL TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Developmental Tox Inhalation (Rat, NOAEL ≥5000 ppm)	2-Butene	107-07-7	SIAP, Butenes/ Robust Summaries for Low 1,3-Butadiene C4 Category, ACC Olefins panel.	Waalkens-Brendsen, DH and JHE Arts. 1992. Combined short term inhalation and reproductive/developmental toxicity screening test with Butene-2 in rats. Proj. #B91-8336 (Study #1410) [2-butene]	
Developmental Tox Inhalation (Rat, NOAEL ≥8000 ppm)	Isobutylene	115-11-7	SIAR, Isobutylene/ Robust Summaries for Low 1,3-Butadiene C4 Category, ACC Olefins panel.	Central Toxicology Laboratory (CTL). 2002. Isobutylene: Prenatal Developmental Toxicity Study in the Rat. CTL/RR0907/Regulatory Report. Cheshire, UK.	
No data – see comments	Acetylene	74-86-2	HPV Test Plan – Acetylene, ACC , 2005		HPV Test Plan indicates that repro dev tox of acetylene is unlikely, therefore no testing has been scheduled.

DEVELOPMENTAL TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
No data	Methane	74-82-8			
Developmental Tox Inhalation (Rat, LOAEL >16,000 ppm; NOAEL = 16, 000 ppm)	Ethane	74-84-0		API HPV study- draft report (OECD 422)	KS=1
Developmental Tox Inhalation (Rat, LOAEL >12,000 ppm; NOAEL = 12, 000 ppm)	n-Propane	74-98-6		API HPV study- draft report (OECD 422)	KS=1
Developmental Tox Inhalation (Rat, LOAEL >9,000 ppm; NOAEL = 9,000 ppm)	n-Butane	106-97-8		API HPV study- draft report (OECD 422)	KS=1
Developmental Tox Inhalation (Rat, LOAEL >9,000 ppm; NOAEL = 3,000 ppm)	Isobutane	75-28-5		API HPV study- draft report (OECD 422)	KS=1; Post-implantation loss observed
Developmental Tox Inhalation (Rat, LOAEL >10,000 ppm; NOAEL = 10, 000 ppm)	LPG	Mixture; mostly propane		API HPV study- draft report (OECD 413/474)	
Developmental Tox Inhalation (Rat, LOAEL >5,000 ppm; NOAEL = 5,000 ppm)	Ethylene	74-85-1	SIAR, Ethylene	Aveyard L. Ethylene: Inhalation (Head-only) Reproduction/Development Toxicity Study in the Rat. Corning Hazleton Report No. 1458/2-1050, April 1996.	
Developmental Tox Inhalation (Rat, LOAEL >10,000 ppm; NOAEL = 10,000 ppm)	Propylene	115-07-1	SIAP, Propylene	BASF Aktiengesellschaft (2002). Propylene - Prenatal developmental inhalation toxicity study in Wistar rats; vapor exposure. Experimental Toxicology and Ecology Laboratory, Rhein, Germany. Project #31R0416/01019.	

DEVELOPMENTAL TOXICITY					
Endpoint	**Component**	**CAS No.**	**Secondary Source**	**Primary Source**	**Comment**
Developmental Tox Inhalation (rat, LOAEL >8,000 ppm for 1-butene and >5000 ppm for 2-butene; NOAELs = 8,000 ppm and 5,000 ppm, respectively)	Butylene	25167-67-3 (mixed isomers)	SIAP, Butenes/ Robust Summaries for Low 1,3-Butadiene C4 Category, ACC Olefins panel.	Waalkens-Brendsen, D.H. and Arts, J.H.E. 1992. Combined short term inhalation and reproductive/developmental toxicity screening test with Butene-2 in rats. Proj. #B91-8336 (Study #1410) [2-butene]	
Developmental Tox Inhalation (Rat, LOAEL >8,000 ppm; NOAEL = 8,000 ppm)	Isobutylene	115-11-7	SIAR, Isobutylene/ Robust Summaries for Low 1,3-Butadiene C4 Category, ACC Olefins panel.	Central Toxicology Laboratory (CTL) (2002). Isobutylene: Prenatal Developmental Toxicity Study in the Rat. CTL/RR0907/Regulatory Report. Cheshire, UK.	
No data – see comments	Acetylene	74-86-2	HPV Test Plan – Acetylene, ACC , 2005		HPV Test Plan indicates that repro dev tox of acetylene is unlikely, therefore no testing has been scheduled.