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US High Production Volume Chemical Program

Category Summary
For
Propylene Streams Category

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Prepared by:

Olefins Panel of the American Chemistry Council

September 9, 2004

EXECUTIVE SUMMARY

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

- Present results of an assessment to determine whether four production streams can be adequately characterized with existing data and additional data as described in the Propylene Streams Category test plan (select human health data for propane from the American Petroleum Institute, Petroleum Gases Category HPV test plan and robust summaries were used to support this assessment).
- Summarize the SIDS (Screening Information Data Set) physicochemical, environmental fate and effects, and human health HPV Program endpoints for the Propylene Streams Category.
- Provide a description of manufacturing processes, potential exposure sources, and uses for Propylene Streams.

The Propylene Streams Category contains four streams. After all data were evaluated to determine whether the streams formed a cohesive category, it was decided that they can be considered a category. The following category report summarizes HPV Program data for the Propylene Streams Category.

The four streams in the Propylene Streams Category can contain as many as five chemical components. Two of the streams comprise relatively pure substances, containing 90.0 to 99.8% propylene. The CAS numbers used to represent the mixed streams in the category are generally vague with respect to the specifics that distinguish the streams within the category. Therefore, more than one CAS number may correctly represent a single stream and a CAS number may be applicable to more than one stream. A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity.

Exposure

The Propylene Streams Category consists of three grades of propylene (plus an additional site-limited, propylene-containing stream that represents a small portion of the category). Essentially all of the 85 billion pounds per year of category production is consumed as a chemical intermediate in other chemical manufacturing processes. The Petroleum Industry produces and uses an approximately equal volume of propylene, but that use and production is not included in this assessment. At ambient conditions, propylene is a gas, therefore inhalation is the most likely route of exposure. Propylene is produced, stored, and transported in closed, pressurized systems and therefore there is no direct worker contact with the stream. Potential for exposure of workers at the olefins process units where propylene is produced occurs because of propylene emissions from fugitive emission sources (equipment leaks) and from other potential emissions from the closed process. Emissions from these sources also present a potential for exposure to the environment and to neighbors bordering production facilities. Similar exposure potentials are expected to exist at the industrial facilities where propylene is converted to the derivative products, but this assessment did not have access to information from those industrial operations. In addition, the assessment did not address the potential exposure to consumers due to propylene residuals in consumer products. Because of the high volatility of propylene, the level of propylene residual in consumer products is expected to be very low, if present at all.

Propylene is listed as a simple asphyxiant by the American Conference of Governmental Industrial Hygienists (ACGIH) who have proposed a TLV (Threshold Limit Value) of 500 ppm. Propylene is a flammable volatile organic compound (VOC) and emissions from industrial facilities are limited both for safety reasons and in compliance with U.S. EPA and state VOC environmental

requirements. The U.S. EPA TRI data indicate industrial emissions of propylene have decreased by 56% since 1988. Propylene is released to the environment from natural sources, including many trees, germinating beans, corn, and cotton and pea seeds. Propylene is a combustion product of gasoline, coal, wood, refuse, and tobacco. It occurs naturally in fruit. Average or mean ambient air concentrations of propylene have been reported in the range of 4 to 17 ppb in urban and industrial areas, and from <0.5 to 3 ppb in rural areas.

Human Health

Propylene and propane have a low order of acute toxicity. As they are both gases at normal temperature and pressure, ingestion or dermal absorption of these materials is unlikely. Inhalation of propylene and propane can produce narcosis and anaesthesia. However, these effects are only seen at very high concentrations (>46,000 ppm to induce narcosis in humans).

In the gaseous state propylene and propane are not irritating to the skin or eyes. However, should skin or eye contact occur to either of these chemicals in their liquid state, tissue freezing, severe cold burn, and/or frostbite may result.

No clinical effects were observed in 14 week and 103 week repeated dose toxicity studies using rats and mice, up to an exposure level of 10,000 ppm. Furthermore, there was no evidence of carcinogenicity in rats and mice exposed to propylene concentrations as high as 10,000 ppm for 103 weeks. Inflammation of the nasal cavity was the only indication of toxicity observed following exposure of male rats to 5,000 and 10,000 ppm propylene and female rats exposed to 10,000 propylene for 103 weeks. These effects were not observed when rats were exposed to similar concentrations for 14 weeks. To further investigate this finding, a recent repeated dose inhalation study indicated no propylene-specific nasal lesions were microscopically detected in any of the male or female exposed to 200; 2000; or 10,000 ppm for 3 or 20 days. No exposure-related inflammation (rhinitis) or alterations (e.g., degeneration, necrosis, hyperplasia, metaplasia) in the squamous, transitional, respiratory, or olfactory epithelium lining the nasal airways were found in any of the sections examined from these propylene-exposed rats. In addition, there were no apparent exposure-related changes, compared to that of controls, in the density of BrdU-labelling in the four specific nasal epithelial populations. These studies demonstrate that propylene produced no clinical effects in rodents exposed to concentrations up to 10,000 ppm, one-half of the lower flammability limit, for up to 14 weeks. However, based on the 103-week repeated dose study in which increased squamous metaplasia and inflammation of the nasal cavities were observed in rats the NOAEL is <5,000 ppm.

Propane was negative for mutagenicity when tested in the *in vitro* Ames assay in five strains of *Salmonella typhimurium*. Propylene induced weak mutagenic activity in one test strain when tested in the *in vitro* Ames *Salmonella* mutagenicity assay at concentrations > 0.25% (2,500 ppm). However, propylene was negative in other Ames assays and in the *in vitro* mouse lymphoma assay. In addition, propylene was negative in two well conducted *in vivo* mutagenicity studies. The NOAEL for *in vivo* mutagenicity is 10,000 ppm.

A prenatal developmental inhalation toxicity elicited no maternal toxicity, prenatal, or developmental toxicity, or teratogenicity at propylene concentrations up to 10,000 ppm, the NOAEL in this study.

Environment

Results of distribution modeling show that chemical constituents of streams in the Propylene Streams Category will partition primarily to the air compartment, with a negligible amount partitioning to water. In the air, these constituents have the potential to rapidly degrade through indirect photolytic processes mediated primarily by hydroxyl radicals. This is expected to be the dominant route of loss and degradation process for constituents of these streams. Aqueous

photolysis and hydrolysis will not contribute to the transformation of category constituents in aquatic environments because they are either poorly or not susceptible to these reactions.

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

Due to the fact that streams in this category are gaseous at ambient temperature and pressure and expected to partition predominantly to the atmosphere, aquatic toxicity testing was not conducted. However, aquatic toxicity was assessed with a model that is based on an equation developed for neutral organic chemicals, a reliable estimation method for the class of chemicals in streams from this category. Calculated toxicity values for two to four day exposures suggest that category members have the potential to produce moderate toxicity, based on an effect range of 10.5 to 100.8 mg/L for selected stream constituents.

**OLEFINS PANEL of the AMERICAN CHEMISTRY COUNCIL
MEMBER COMPANIES**

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

* Companies that are part of the Olefins Panel, but do not produce substances in the Propylene Streams Category.

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1 CATEGORY DESCRIPTION AND JUSTIFICATION

1.1 Category Identification

For purposes of the US High Production Volume (HPV) Chemical Challenge Program (Program), the Propylene Streams Category test plan submitted in November 2001 (Olefins Panel, HPV Implementation Task Group, 2001) included four production streams that are represented by two Chemical Abstracts Service (CAS) registration numbers (RNs). In addition, the stream designated "Propylene Stream" is sometimes represented using the CAS numbers of the stream constituents, propylene, ethane, and propane (Table 1).

The test plan identified existing data and additional sources of data, based on an extensive technical review of the category, to adequately characterize the four streams for the HPV Program endpoints. Additional data sources included select human health data for propane from the American Petroleum Institute (API), Petroleum Gases Category HPV test plan and robust summaries (API, 2000).

After all data were evaluated to determine whether the streams formed a cohesive category, it was decided that they can be considered a category. The following category report summarizes HPV Program data for the Propylene Streams Category. The four streams in the Propylene Streams Category can contain as many as five chemical components. Two of the streams are relatively pure substances, containing 90.0 to 99.8% propylene. A process stream is a mixture of chemicals that arises from a chemical reaction or separation activity.

Table 1. Production Streams, CAS RNs, and CAS RN Names in the Propylene Streams Category

Production Streams	CAS RN	CAS RN Name
Propylene, Polymer Grade	115-07-1	1-Propene
Propylene, Chemical Grade	115-07-1	1-Propene
Propylene Stream	115-07-1, 74-84-0, 74-98-6	Mixture of 1-Propene, Ethane, and Propane
	68606-26-8	Hydrocarbons, C3
Light Ends from Butadiene Plant	68606-26-8	Hydrocarbons, C3

Note: The definitions found in the TSCA Chemical Substance Inventory for the CAS RNs in this category are vague with respect to composition. Therefore, it is not uncommon to find that one CAS RN is correctly used to describe different streams (different compositions) or that two or more CAS RNs are used to describe one stream (similar composition).

The streams in this category include hydrocarbon reaction products and relatively pure hydrocarbons with a carbon number distribution that is predominantly C3. These streams all contain significant levels of propylene. The typical compositions of the streams in this category are shown in Table 2.

Table 2. Typical Constituent (wt%) Range in Streams of the Propylene Streams Category

Constituent	Propylene, Polymer Grade (wt %)	Propylene, Chemical Grade (wt %)	Propylene Stream (wt %)	Light Ends from Butadiene Plant (wt %)
Methane		0.5		
Ethylene		0.1 - 1		
Ethane		0.1 - 1		0 - 2
Propylene	95 - 100	90 - 99.8	85	25 - 40
Propane	0.1 - 0.5	0.2 - 10	12	60 - 70
Methylacetylene & Propadiene			3	

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

Note: One manufacturer reported the lower limit value of 95% propylene for Polymer Grade Propylene. Typically, and as reported by all other reporting producers, Polymer Grade Propylene contains 99 to 100% propylene.

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

The Propylene Streams Category streams arise from production processes associated with ethylene manufacturing (see Appendix I for a description of the ethylene and associated processes). Briefly, descriptions of the four process streams are:

1. Propylene, Polymer Grade stream is a high purity (typically 99%+) product of the ethylene unit. It is obtained by fractionation of a portion of the condensed cracking furnace effluent and other processing steps (e.g. C3 acetylene removal). The final polymer grade propylene is produced as the distillate from the C3 splitter and can contain a small amount of propane.
2. Propylene, Chemical Grade stream is a C3 product with typical propylene content of 93 to 95%. Propane accounts for most of the balance of the composition. An ethylene process using a scheme similar to that used for polymer grade propylene, but with fewer or less rigorous purification steps, produces this grade.
3. Propylene Stream is the C3 stream prior to separation into propylene and propane. Typically, this stream is produced as the overhead from the depropanizer in an ethylene unit. It is a narrow boiling-range mixture that consists predominantly of C3 hydrocarbons. A typical composition is 85% propylene, 12% propane, and 3% C3 acetylenes.
4. Light Ends from Butadiene Plant stream is produced by fractionation of the C4 Crude Butadiene stream to remove relatively low levels of propane and propylene that may be contained in the stream. The carbon number distribution for the stream is predominantly C3.

1.2 Purity/Impurities/Additives

Typically, additives are not added to propylene streams prior to shipment.

1.3 Physico-Chemical Properties

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

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

Chemical	Melting Point (°C)	Boiling Point (°C @760 mmHg)	Vapor Pressure (hPa@ 25 °C)	Log K _{ow}	Water Solubility (mg/L @25°C)
Propadiene	-132.9	-18.32	6.71 E3	1.65	1,449
Propylene	-135.4	-9.84	9.31 E3	1.68	1,162
Propane	-133.9	-7.76	8.19 E3	1.81	1,088

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

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

Chemical	Melting Point (°C)	Boiling Point (°C @760 mmHg)	Vapor Pressure (hPa@ 25 °C)	Log K _{ow}	Water Solubility (mg/L @25°C)
Propadiene	-136.2	-34.4	7.24 E3	1.45	2,147
Propylene	-185.2	-47.6	1.16 E4	1.77	200
Propane	-187.6	-42.1	9.53 E3	2.36	369

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

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

1.3.1 Melting Point (Range)

Based on calculated values, the streams in this category can have a melting point range of -135.4 to -132.9 °C. Based on measured values, the streams in this category can have a melting point range of -187.6 to -136.2 °C. The measured data demonstrate a wider range than the calculated data, although they overlap. The measured data are considered the appropriate primary data set to characterize the melting point range of category members.

1.3.2 Boiling Point (Range)

Based on calculated values, the streams in this category can have a boiling point range of -18.32 to -7.76 °C. Based on measured values, the streams in this category can have a boiling point range of -47.6 to -34.4 °C. The calculated data are not comparable with the measured data. The measured data are consistent with process knowledge and are considered the appropriate primary data set to characterize the boiling point range of category members.

1.3.3 Vapor Pressure (Range)

Based on calculated values, the streams in this category can have a vapor pressure range of 6.71 E3 to 9.31 E3 hPa at 25 °C. Based on measured values, the streams in this category can have a vapor pressure range of 7.24 E3 to 1.16 E4 hPa at 25 °C. The calculated data compare favorably with the measured data. The measured data are consistent with process knowledge and are considered the appropriate primary data set to characterize the vapor pressure range of category members.

1.3.4 Log K_{ow} (Range)

Based on calculated values, the streams in this category can have a log K_{ow} range of 1.65 to 1.81. Based on measured values, the streams in this category can have a log K_{ow} range of 1.45 to 2.36. The calculated data compare favorably with the measured data. The measured data are considered the appropriate primary data set to characterize the log K_{ow} range of category members.

1.3.5 Water Solubility (Range)

Based on calculated values, the streams in this category can have a water solubility range of 1,088 to 1,449 mg/L. Based on measured values, the streams in this category can have a water solubility range of 200 to 2,147 mg/L. The measured data demonstrate a wider range than the calculated data, although they overlap. The measured data are considered the appropriate primary data set to characterize the water solubility range of category members.

1.4 Category Justification

The data used to characterize the human health endpoints of the streams in this category include data on the major C3 components including propylene and propane. At the time of this document's preparation, propylene and propane had been sponsored in the OECD SIDS and Petroleum HPV Test Group programs, respectively, and as such, data are available for these substances through these programs.

The components of the Propylene Streams Category, primarily propylene and propane, are non-polar narcotics that act as anaesthetics and have comparatively low toxicity. The approach to assess the human health endpoints for this category uses propylene data to characterize streams that are predominantly propylene and propane data to characterize the mixed streams.

The strength of the propylene toxicological data includes a long-term (lifetime), controlled exposure study in rats and mice in which no increase in tumors was seen at any dose level. The only effects reported were low-grade irritation to the nasal cavity in rats and mice and a questionable inflammatory change in the mouse kidney.

2 EXPOSURE AND USE

The Category and Stream Production

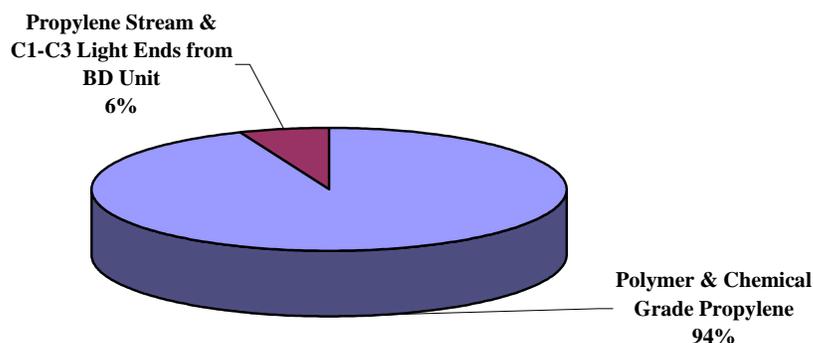
The Propylene Streams Category contains four CAS RNs (Table 1) that are associated with the following four process streams:

- Propylene, Polymer Grade
- Propylene, Chemical Grade
- Propylene Stream
- Light Ends from Butadiene Plant

These first three streams above are manufactured in ethylene production units and the last is produced by the butadiene plant (see Appendix I). Propylene produced by the ethylene industry accounts for approximately 50% of annual propylene stream production in the US, with petroleum

refineries accounting for the balance of the production. The Propylene Streams Category was defined by grouping the Olefins Industry's commercial streams that contain propylene. The CAS RNs in the category are 115-07-1, 74-84-0, 74-98-6, and 68606-26-8. The category consists of propylene, produced as either polymer or chemical grades, or infrequently as an intermediate propylene-propane stream. An additional stream, a propylene-containing C1-C3 Light Ends, generated from processing the ethylene process-derived C4 Crude Butadiene stream, is included in the category. Distribution of the 85 billion pounds/year of category production¹ among the category streams is shown in Figure 1.

Figure 1. Propylene Streams Category Production by Stream



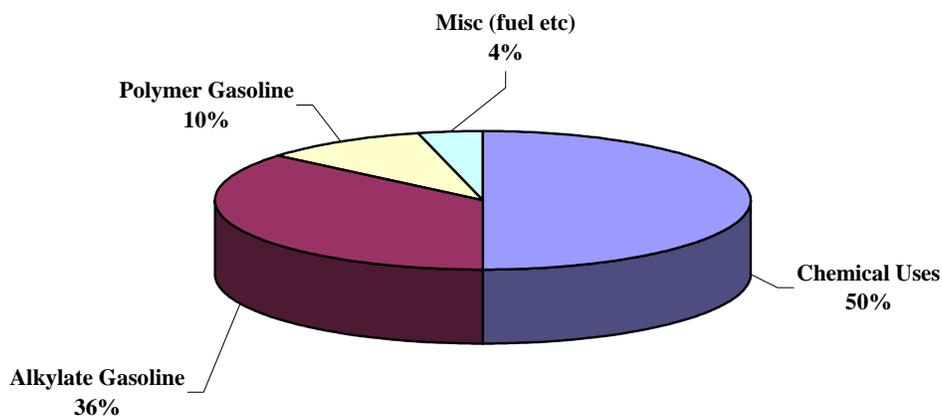
Transportation of Category Streams

When shipped between industrial sites, propylene is transported in pressurized, closed systems by pipeline, pressure barge, tank car, and less frequently by tank truck. Propylene is transported as a pressurized gas or as a liquid at ambient temperature and approximately 250 psig or higher pressure.

Propylene Use

Propylene is a major chemical intermediate. The primary uses (Hazardous Substances Databank, 2003) of propylene are shown in Figure 2.

¹ 85 billion lbs/yr is the total commercial production of category streams reported by participants in the HPV Propylene Streams Category, and based on their 1998 TSCA IUR report. Figure 1 does not include propylene produced by the petroleum industry.

Figure 2. Chemical and Gasoline Uses of Propylene (1974)

The major chemical uses of propylene are shown in Figure 3 (Chemical Market Reporter, 2003).

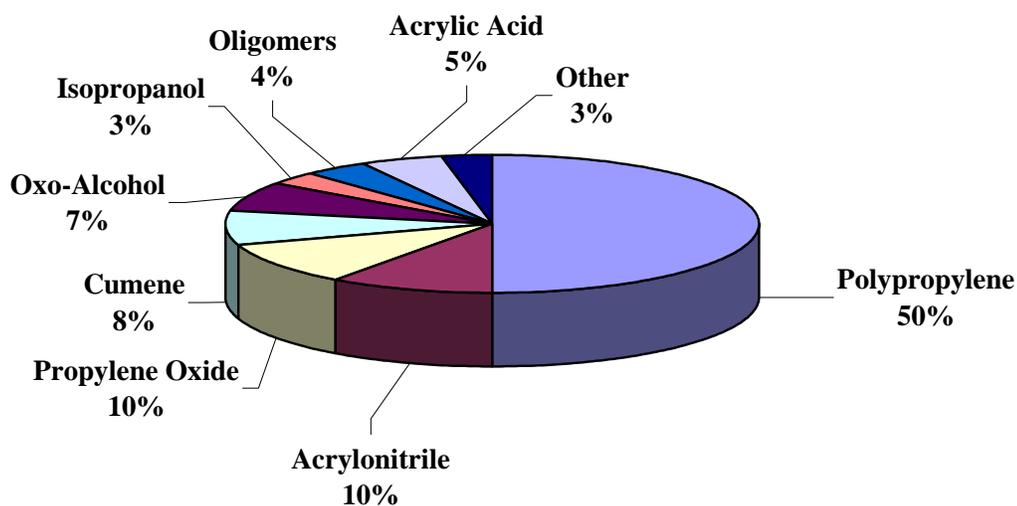
Figure 3. Chemical Uses of Propylene

Figure 2 includes propylene produced and used in the petroleum industry as an alkylation or polymer-gasoline feedstock. Production of refinery grade propylene and the use of that stream are not included in this exposure assessment. As shown in Figure 2, gasoline and fuel use account for about 50% of total propylene consumption. Figure 3 provides 2003 data on industrial chemical uses of propylene. Figure 3 represents the use of propylene included in this HPV category. Propylene is sometimes used as a refrigerant in industrial refrigeration systems, which is the case in the ethylene process. Propylene is reported to be used as a propellant or component in aerosols, and propylene may be present at low levels in fuel gases (Hazardous Substances Databank, 2003).

Route of Potential Exposure

Because propylene is a gas at ambient conditions, the most likely route of exposure to propylene is inhalation (Hazardous Substances Databank, 2003).

Sources of Exposure

Exposure to propylene is limited for workers at ethylene plants where the streams in this category are manufactured because that equipment and those processes use closed systems. For the industrial workers at these facilities, the most likely exposure potential occurs through inhalation of low-level concentrations in air of vapors that escape from the closed process, such as fugitive emissions from valve packing and pump seals. Other potential exposures may result during operations such as sampling, connecting and disconnecting bulk transportation vessels (tank cars and pressure barges); or during infrequent opening of equipment for maintenance; or from episodic emissions to the air from the process cooling tower water systems; or emissions of propylene from control devices, such as flares.

Similar exposure potential is expected to exist at the industrial facilities where propylene is converted to the derivative products, but this assessment did not have access to information from those industrial operations.

The above sources of Propylene emissions present a potential for exposure to the public and to the environment adjacent to the industrial facilities that use or produce propylene.

The assessment did not address the potential exposure to consumers due to propylene residuals in consumer products that are produced from propylene. Because of the high volatility of propylene, the level of propylene residual in consumer products is expected to be very low, if present at all.

Some sources (Hazardous Substances Databank, 2003) of propylene are biological in origin; it is a component of garlic essential oils, European fir, Scots pine, natural gases, and it is released by germinating beans, corn, cotton, and pea seeds. Propylene's release to the environment is wide spread since it is a ubiquitous product of incomplete combustion. Propylene is released to the atmosphere in emissions from the combustion of gasoline, coal, wood, refuse, and tobacco. Propylene occurs naturally in fruit, such as bananas and apples, and also in ocean sediments as a degradation product of microbial action.

Controls that Limit Exposure

The ACGIH lists propylene as a simple asphyxiant and has proposed (ACGIH, 2004) a TLV of 500 ppm as an 8-hr TWA.

Flammability of propylene vapors provides major incentive to limit emissions from process equipment at industrial facilities.

Propylene is a volatile organic compound (VOC) and is subject to USEPA and state environmental regulations that limit VOC emissions. The USEPA new source performance standards of 40CFR Part 60 limit emissions of VOC at new or modified Olefins process units where the streams in this category are produced. Subpart VV of 40CFR Part 60 limits emission from equipment leaks, Subpart NNN limits emissions from distillation operations, subpart RRR limits emissions from reactor systems and subpart DDD limits emissions from the Polymer Manufacturing Industry. Facilities that produce and use propylene are also typically subject to state operating permits and regulations that further limit VOC emissions.

Ambient Air Concentration Data

Averages of data (Air Toxics Monitoring Network, 1992-1997) that was calculated from published ambient propylene concentrations measured at various industrial sites in Texas (1994 through 1997) indicate 24-hour annual high propylene concentrations averaging 14.5 ppb (range 0 to 80 ppb) and annual means averaging 3.1 ppb (range 0 to 14 ppb).

Ground-level concentrations (Hazardous Substances Databank, 2003) of propylene in urban air samples collected in several US sites ranged from 4 to 17 ppb (geometric means), whereas concentrations in rural surface air samples from six domestic sites ranged from <0.5 to 3.0 ppb (geometric means) (US EPA, 1986).

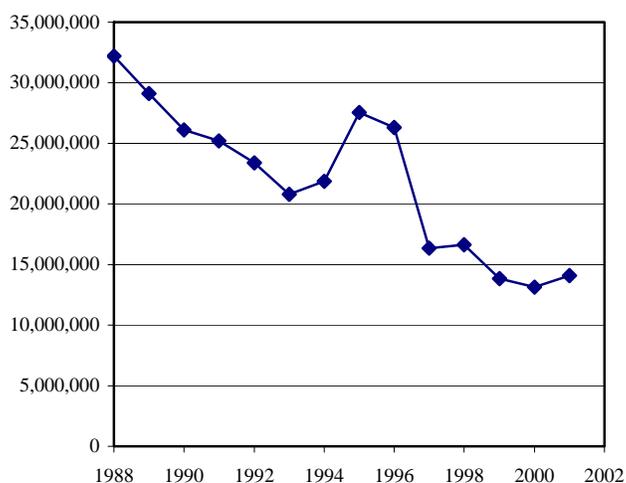
Estimates of Number of Potentially Exposed Workers

Estimates (Hazardous Substances Databank, 2003) of occupational exposure to propylene have been reported in industrial hygiene surveys performed by the National Institute for Occupational Safety and Health (NIOSH). NIOSH, in a 1972-1974 NATIONAL OCCUPATIONAL HAZARD SURVEY, statistically estimated that 10,274 workers are potentially exposed to propylene in the USA, and in a National OCCUPATIONAL EXPOSURE SURVEY FOR 1981 to 1983, NIOSH statistically estimated that 7,305 workers are potentially exposed to propylene in the USA.

Propylene Emissions

Industrial emissions of propylene are reported to the EPA and made available to the public in the Toxics Release Inventory (TRI) (EPA website for TRI: <http://www.epa.gov/tri/>). This inventory was established under the Emergency Planning and Community Right-to-Know Act of 1986 (EPCRA) and expanded by the Pollution Prevention Act of 1990. The TRI data indicate that industrial emissions of propylene have significantly decreased since 1988 (Figure 4). The TRI data from 2001 indicate that emissions of propylene reported in the TRI report have declined by 56% since 1988.

Figure 4. TRI Propylene Emissions (lbs/year) 1988-2001



Summary of Exposure Assessment

The Propylene Streams Category consists of three grades of propylene (plus an additional site-limited, propylene-containing stream that represents a small portion of the category). Essentially all of the 85 billion pounds per year of category production is consumed as a chemical intermediate in other chemical manufacturing processes. The Petroleum Industry produces and uses an approximately equal volume of propylene, but that use and production is not included in this assessment. At ambient conditions, propylene is a gas, therefore inhalation is the most likely route of exposure. Propylene is produced, stored, and transported in closed, pressurized systems and therefore there is no direct worker contact with the stream. Potential for exposure of workers at the olefins process units where propylene is produced occurs because of propylene emissions from fugitive emission sources (equipment leaks) and from other potential emissions from the closed process. Emissions from these sources also present a potential for exposure to the environment and to neighbors bordering production facilities. Similar exposures potentials are expected to exist at the industrial facilities where propylene is converted to the derivative products, but this assessment did not have access to information from those industrial operations. In addition, the assessment did not address the potential exposure to consumers due to propylene residuals in consumer products. Because of the high volatility of propylene, the level of propylene residual in consumer products is expected to be very low, if present at all.

Propylene is listed as a simple asphyxiant by ACGIH, with a proposed TLV of 500 ppm. Propylene is a flammable volatile organic compound (VOC) and emissions from industrial facilities are limited both for safety reasons and in compliance with U.S. EPA and state VOC environmental requirements. The U.S. EPA TRI data indicate industrial emissions of propylene have decreased by 56% since 1988. Propylene is released to the environment from natural sources, including many trees, germinating beans, corn, and cotton and pea seeds. It is a combustion product of gasoline, coal, wood, refuse, and tobacco. It occurs naturally in fruit. Average or mean ambient air concentrations of propylene have been reported in the range of 4 to 17 ppb in urban and industrial areas, and from <0.5 to 3 ppb in rural areas.

3 ENVIRONMENTAL FATE

3.1 Photodegradation

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

3.1.1 Direct Photodegradation

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

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

The stratospheric ozone layer prevents UV light of less than 290 nm from reaching the earth's surface. Therefore, only light at wavelengths between 290 and 750 nm can result in photochemical transformations in the environment (Harris, 1982a). Although the absorption of UV light in the 290-750 nm range is necessary, it is not always sufficient for a chemical to undergo photochemical degradation. Energy may be re-emitted from an excited molecule by mechanisms other than chemical transformation, resulting in no change to the parent molecule.

A conservative approach to estimating a photochemical degradation rate is to assume that degradation will occur in proportion to the amount of light at wavelengths >290 nm absorbed by the molecule (Zepp and Cline, 1977). Saturated hydrocarbons, like propane, do not absorb light above 200 nm. Characteristic absorbance maxima (λ_{\max}) and associated molar absorptivities (ϵ) for two unsaturated hydrocarbons that are not constituents of this category, but are used as examples of chemicals containing double bonds, are listed in Table 5 (Harris, 1982a). The constituents of streams in the Propylene Streams Category would have absorbance maxima and associated molar absorptivities in the range of those chemicals in Table 5.

Table 5. Characteristic Absorbance Maxima (λ_{\max}) and Associated Molar Absorptivities (ϵ) for Two Unsaturated Hydrocarbons

Hydrocarbon	λ_{\max} *	ϵ
Ethylene	193	10,000
1,3-Butadiene	217	20,900

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

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

3.1.2 Indirect Photodegradation

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

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

Since the reactions necessary for this degradative process only take place in the presence of sunlight, the atmospheric half-lives are normalized for a 12-hour day. The three chemicals selected to represent the atmospheric half-life range of streams in this category are C3 hydrocarbons that are predominant among the four CAS RNs (Table 6).

Atmospheric oxidation via hydroxyl radical attack can be a significant route of degradation for streams in this category. Based on calculated values, chemicals in streams from this category can have an atmospheric half-life range of 4.9 to 101.2 hours as a result of indirect photolysis by hydroxyl radical attack.

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

Chemical	Calculated Half-life* (hrs)	OH ⁻ Rate Constant (cm ³ /molecule-sec)
Propadiene	13.1	9.8 E-12
Propylene	4.9	24.6 E-12
Propane	101.2	1.3 E-12

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

3.2 Stability in Water (Hydrolysis)

Hydrolysis of an organic molecule occurs when a molecule (R-X) reacts with water (H₂O) to form a new carbon-oxygen bond after the carbon-X bond is cleaved (Gould, 1959; Harris, 1982b). Mechanistically, this reaction is referred to as a nucleophilic substitution reaction, where X is the leaving group being replaced by the incoming nucleophilic oxygen from the water molecule. The leaving group, X, must be a molecule other than carbon because for hydrolysis to occur, the R-X bond cannot be a carbon-carbon bond.

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

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

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

3.3 Distribution in the Environment

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

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

The three chemicals selected to characterize the transport/distribution range are C3 hydrocarbons that are predominant across the streams in this category. Physical property data (Table 4) used in the model are from the EPIWIN (1999) database.

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

Chemical	Distribution Per Environmental Compartment (%)					
	Air	Water	Soil	Sediment	Suspended Sediment	Biota
Propadiene	99.96	0.04	<0.01	<0.01	<0.01	<0.01
Propylene	99.99	0.01	<0.01	<0.01	<0.01	<0.01
Propane	99.47	0.43	<0.1	<0.01	<0.01	<0.01

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

3.4 Biodegradation

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

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

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

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

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

Streams from the Propylene Streams Category do not lend themselves to being evaluated for biodegradability using standard experimental designs because of their physical state. However, there is microbial metabolism information for selected constituents in this category that demonstrates they have the potential to biodegrade. The sections immediately below summarize results of studies for the two predominant constituents from this category. The data do not allow for

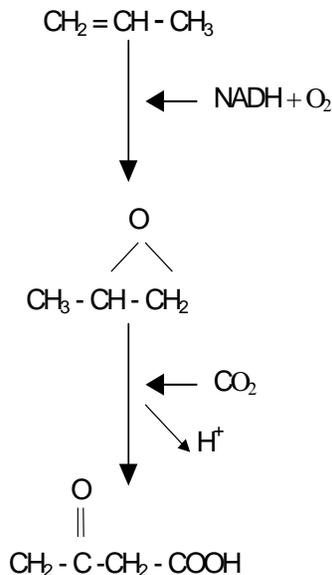
an estimation of the extent of biodegradability relative to a standard 28-day test procedure using a microbial inoculum from a wastewater treatment facility. However, the constituents discussed below are predicted by BIOWIN, Biodegradation Probability Program (EPIWIN, 1999), as having the potential to biodegrade rapidly. [BIOWIN is a model in EPIWIN that calculates the probability of an organic chemical to rapidly biodegrade by a mixed population of microorganisms. BIOWIN can also estimate the time required to meet primary and ultimate biodegradation criteria.]

3.4.1 Propylene Biodegradation

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

Two pathways for the aerobic metabolism of propylene have been described (van Agteren *et al.*, 1998) that include the formation of either 1,2-propanediol or acetyl CoA prior to mineralization to CO₂. Results of experimental studies identified a catabolic pathway for propylene (Figure 4) as mediated by a *Xanthobacter* sp. (Small *et al.*, 1995).

Figure 4. Microbial Metabolic Pathway for the Degradation of Propylene by a *Xanthobacter* sp.



The degradation of propylene by a *Xanthobacter* sp. leads to acetoacetate, which is an entry compound into intermediary metabolism.

3.4.2 Ethylene and Propane Biodegradation

The potential biodegradability of other components including ethylene and propane has been summarized and metabolic pathways leading to their biodegradation have been described (van Agteren *et al.*, 1998; Hartmans, 1993). These compounds have been shown to biodegrade to high extents such that if they were to partition to either a terrestrial or aqueous environment, they would be subject to biodegradative processes that would result in their removal from the environment.

3.4.3 Abiotic and Biotic Degradation Summary

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

4 HUMAN HEALTH HAZARDS

4.1 Effects on Human Health

4.1.1 Toxicokinetics, Metabolism, and Distribution

The pharmacokinetics and metabolism of propylene have been studied in rats and mice. Only about 16% of inhaled propylene is systemically available (Golka *et al.*, 1989). Propylene is excreted primarily by exhalation. Metabolic elimination of propylene by rats and mice follows first-order kinetics. Metabolism of propylene is saturated at inhaled concentrations greater than 500 ppm in the rat and 1,600 ppm in the mouse (Svensson and Osterman-Golkar, 1984; Golka *et al.*, 1989). When steady-state conditions are established at ambient concentrations of propylene below 100 ppm, the fraction of systemically available propylene metabolized in the rat is approximately 58% (Golka *et al.*, 1989). One reference was found on propylene metabolism in humans; this abstract describes the presence of low levels of propylene oxide (approximately 0.2 ppb) in the expired air of one individual continuously exposed to 25 ppm propylene for up to 4.5 hours (Filser *et al.*, 1997, abstract cited in Filser *et al.*, 2000). Thus, it was suggested that propylene is metabolized to propylene oxide in humans². Propylene oxide has been classified as a Group 2B carcinogen by IARC; the agent (mixture) is possibly carcinogenic to humans (IARC, 1994). The metabolism of propylene to propylene oxide has raised questions that propylene may be a procarcinogen. However, there is evidence to refute this view including 2 negative bioassays (Quest *et al.*, 1984; Ciliberti *et al.*, 1988) and IARC has determined that propylene (mixture or exposure circumstance) is not classifiable as to its carcinogenicity to humans (Group 3, IARC, 1994).

Svensson *et al.* (1991) determined that propylene oxide was the principal metabolite of propylene in male CBA mice that inhaled 230; 680; 22,100; or 30,000 ppm [¹⁴C] labeled propylene for 6 to 7 hours. Similar levels of hemoglobin adducts were formed after inhalation of propylene or after injection of calculated equivalent doses of propylene oxide. After exposure to a high propylene concentration (not specified, but estimated to be >20,000 ppm from the limited data provided) the distribution of N-7 hydroxypropyl guanine adducts observed in the liver, testes, spleen, lung, and kidney and haemoglobin adducts at termination of exposure was qualitatively similar to but

² Methyl oxirane (Propylene oxide, CAS No. 75-56-9) was assessed at SIAM 13, 6-9 November 2001 with UK as sponsor country. It has been the subject of an EU risk assessment. A full copy of the final report is available at: http://ecb.jrc.it/DOCUMENTS/Existing-chemicals/RISK_ASSESSMENT/DRAFT/R016_0002_env_hh.pdf

quantitatively less than that formed by injection of 0.07 to 0.19 mmol/kg body weight of propylene oxide.

Golka *et al.* (1989) compared the pharmacokinetics of propylene and propylene oxide in rats as part of an investigation into the differences in carcinogenicity between these two compounds. Sprague-Dawley rats were exposed to either propylene or propylene oxide; a two-compartment model was used to determine pharmacokinetic parameters. The thermodynamic equilibrium constant for the whole body to air ratio was determined to be 1.6 for propylene and 45 for propylene oxide. Propylene exhibited saturation kinetics according to Michaelis-Menten starting at about 50 ppm but propylene oxide did not exhibit saturation up to concentrations of 3,000 ppm in the exposure chamber. It was found that starting at 50 ppm, only about 16% of propylene was absorbed; of the 16% absorbed, almost one-half is exhaled and the remainder is oxidized to propylene oxide (a saturable reaction). In contrast, most of the inhaled propylene oxide is metabolized (about 96%), with only small amounts exhaled unchanged. Golka *et al.* (1989) calculated that an inhaled propylene oxide concentration of 100 ppm the body burden of propylene oxide would be 124 nl gas/ml tissue in rats. However, the maximum oxide body burden that propylene can reach is 71 nl gas/ml tissue, even if animals are exposed to very high concentrations. When this is compared to the carcinogenicity NOAEL of 200 ppm for propylene oxide (Kuper *et al.*, 1988), this provides a mechanistic basis that explains why no increase in cancer has been observed at 5,000 and 10,000 ppm propylene in chronic animal inhalation studies.

Maples and Dahl (1991) found that exposure to 6 ppm propylene for 6 hours produced 160 ng propylene oxide per gm of blood in rats and that 600 ppm propylene for 8 hours produced 740 ng propylene oxide per gram of blood. Both exposure concentrations reduced nasal and liver cytochrome P-450 levels (to differing degrees).

A physiological toxicokinetic model (PT model) was developed for inhaled propylene gas in mouse, rat and human (Filser *et al.*, 2000). Metabolism was simulated to occur in the liver (90%) and in the richly perfused tissue group (10%). Tissue: air partition coefficients were determined *in vitro* using tissues of mice, rats, and humans. For male B6C3F₁ mice and male Fischer 344/N rats, parameters of propylene metabolism were obtained from gas uptake experiments. Preliminary toxicokinetic data on propylene metabolism in humans were obtained in one volunteer who was exposed up to 4.5 hr to constant concentrations of 5 and 25 ppm propylene (Filser *et al.*, 1997, abstract cited in Filser *et al.*, 2000). The PT model was used to calculate propylene blood concentrations at steady state. Maximum rates of metabolism were 110 $\mu\text{mol/h/kg}$ in mice and 50.4 $\mu\text{mol/h/kg}$ in rats. At 25 ppm, the blood values were comparable across species, with 0.19, 0.32, and 0.34 $\mu\text{mol/L}$ for mouse, rat, and human, respectively. However, the corresponding rates of propylene metabolism differed dramatically, being 8.3, 2.1 and 0.29 $\mu\text{mol/h/kg}$ in mouse, rat, and human. For a repeated human exposure to 25 ppm propylene in air (8 hours/day, 5 days/week), propylene concentrations in venous blood were simulated. The prediction demonstrates that propylene is eliminated so rapidly in humans that it cannot accumulate. For low exposure concentrations, the rate of uptake into blood by inhalation is limited by the blood flow through the lung and the rate of metabolism is limited by the blood flow through the metabolising organs (Filser *et al.*, 2000).

Conclusion

Propylene exhibits saturation kinetics according to Michaelis-Menten. Golka *et al.* (1989) found that starting at 50 ppm propylene concentration, only about 16% of propylene was absorbed; of the 16% absorbed, almost one-half is exhaled and the remainder is oxidized to propylene oxide (a saturable reaction). Golka *et al.* (1989) calculated the body burden of propylene oxide would be 124 nl gas/ml tissue at 100 ppm propylene oxide exposure concentration. However, the maximum oxide

body burden from propylene exposure that can be reached is 71 nl gas/ml tissue, even if animals are exposed to very high concentrations of propylene (Golka *et al.*, 1989). Preliminary data from inhalation exposures at 25 ppm propylene with one human volunteer indicate that about 35% of the inhaled propylene is taken up into the body and only about 20% of this is metabolized; from these data, it can be calculated that about 7% of the inhaled propylene is metabolized in humans, with the rest exhaled unchanged (Filser *et al.*, 2000).

4.1.2 Acute Toxicity

Studies in Animals

Propylene

There are several acute toxicity studies described in the dossier, all of which were by inhalation. Since propylene is a gas at normal temperature and pressure, ingestion of this material is unlikely, as is dermal absorption. Thus, no acute oral or dermal toxicity studies have been conducted on this material. Although the two studies described in the BIBRA status report on propylene (1976) are old (Brown, 1924; Halsey *et al.*, 1926) and predate standard guidelines, there is adequate information when they are considered in combination to address the acute inhalation toxicity of propylene. However, there is more information presented on these acute studies than on any of the other studies listed.

Acute rodent inhalation studies were conducted with propylene (Halsey *et al.*, 1926). In these studies propylene concentrations of 30 to 40% (300,000 to 400,000 ppm) were minimally anaesthetic. Concentrations of 55 to 65% propylene were lethal to mice; however, dogs could tolerate 50% for hours without apparent depression of circulation or respiration, and the lethal dose in dogs and cats was between 70 and 80% (Halsey *et al.*, 1926). In other studies, inhalation of 65,000 ppm propylene for 4 hours by Sprague-Dawley rats did not produce death or hepatotoxicity (the liver was the only organ examined) (Conolly and Osimitz, 1981). Inhalation of 50,000 ppm for four hours also did not produce death or hepatotoxicity, unless the Sprague-Dawley rats were pre-treated with the PCB Arochlor 1254, in which case liver toxicity after Arochlor pre-treatment was manifested by increased liver weights, areas of macroscopic haemorrhage, and elevated liver enzymes (Osimitz and Conolly, 1985).

As early as 1924 it was known that propylene had anaesthetic properties on cats: concentrations of 37% propylene in oxygen or air induced narcosis. Symptoms of anaesthesia occurred within two minutes of exposure at 70% propylene but the cats recovered quickly with no apparent lasting effects (Brown, 1924). Additional acute inhalation studies were conducted with propylene in cats. No toxic signs or symptoms were observed when anaesthesia was maintained at propylene concentrations of 20% to 31% (i.e., 200,000 to 310,000 ppm, v). Some subtle effects were observed at concentrations ranging from 40% to 50% (i.e., 400,000 to 500,000 ppm) and blood pressure decreases and rapid pulse occurred at a concentration of 70% (i.e., 700,000 ppm). An unusual ventricular ectopic beat was observed with exposures from 50% to 80% (500,000 to 800,000 ppm). In summary, in this study exposure of cats to 40 to 50% propylene caused narcosis, while exposure to 50 to 80% propylene caused lethality (Brown, 1924).

The estimated propylene concentration for onset of narcosis in humans is 46,000 ppm (Drummond, 1993). The asphyxiation limit for propylene is estimated to be 236,000 ppm, the level that will dilute the normal concentration of oxygen in air to approximately 16% (calculated by EMBSI). Both of these concentrations are above the lower flammability level for propylene of 20,000 ppm.

Propane

An acute LC₅₀ inhalation study was conducted with propane in rats (Clark and Tinson, 1982). In this study, groups of either 6 male or 6 female rats were exposed to propane for 15 minutes in 500 ml whole body chambers. A range of propane concentrations were tested in order to calculate the

concentration required to produce effects on the central nervous system (CNS) in 50% of the exposed animals, i.e., EC₅₀. The concentration required to cause death after a 15 minute exposure was also determined and the 15-minute LC₅₀ was calculated. Propane caused CNS depression. Signs of intoxication included slight ataxia, loss of righting reflex, loss of movement, narcosis, shallow respiration and eventually death from respiratory depression. Recovery from a non-lethal exposure was rapid and the rats appeared normal within 10 minutes. Where death occurred, it was during exposure, never afterwards. The calculated 10-minute EC₅₀ for CNS depression was approximately 280,000 ppm (220,000 to 350,000 ppm) and the 15-minute LC₅₀ was calculated to be >800,000 ppm.

The estimated propane concentration for onset of CNS depression in humans is 47,000 ppm whereas the asphyxiation limit is estimated to be 140,000 ppm (Drummond, 1993). Both of these are above the lower explosive limit (LEL) for propane of 21,000 ppm.

Conclusion

Propylene and propane have a low order of acute toxicity by the inhalation route of exposure. They are both asphyxiants at high concentrations producing a dilution or displacement of oxygen in air. The asphyxiation limits for propylene and propane in humans have been estimated to be approximately 23.6% and 14% (i.e., 236,000 ppm and 140,000 ppm), respectively. The lower explosive limits for propylene and propane are 2% and 2.1% (i.e., 20,000 ppm and 21,200 ppm), respectively. Thus, the explosive range of airborne concentrations for both propylene and propane are reached before any acute physiologic effects can be manifested.

Table 8. Summary of Acute Inhalation Toxicity Data for the Propylene Streams Category

CAS RN and Substance Name	Test Organism	Exposure Duration (hr)	LC ₁₀₀ (ppm)
115-07-1 Propylene	Mouse	Unknown	550,00 to 650,000
115-07-1 Propylene	Dog	Unknown	700,000 to 800,000
115-07-1 Propylene	Cat	Unknown	700,000 to 800,000
115-07-1 Propylene	Rat	4	>65,000*
74-98-6 Propane	Rat	0.25	>800,000*

* LC₅₀ (ppm)

4.1.3 Irritation

Skin/Eye Irritation

There are no animal studies on skin or eye irritation. However, insight to potential effects from members of this category for these endpoints is provided by examining the 14-week and 2-year NTP (1985) studies in rats and mice and the 4-week DuPont (2002a) study in rats (discussed below in sections 4.1.4 and 4.1.6) that were conducted with propylene. Inflammation was observed in the nasal cavities in the 2-year study, probably due to mild irritant properties of the inhaled gas at concentrations >5,000 ppm. However, no inflammation or irritation in the nasal cavities was observed in the 14- or 4-week studies.

Rapid evaporation of liquid propylene may freeze the skin and cause "frost bite"; however, the gas produces little or no irritation (BIBRA, 1989).

4.1.4 Repeated Dose Toxicity

The National Institutes of Health has conducted several repeated dose toxicity studies on propylene as part of the National Toxicology Program (NTP, 1985). These studies were conducted using protocols comparable to OECD test guidelines, in accordance with GLP methods and were therefore selected as the critical studies.

Fischer-344 (F344/N) rats (9 to 11/sex/group) were exposed by inhalation for 6 hours/day, 5 days/week for 14 weeks to 0; 625; 1,250; 2,500; 5,000; or 10,000 ppm propylene in air. Individual clinical observations were made daily. Body weights were recorded prior to exposure and at sacrifice (NTP, 1985). No compound related deaths or clinical signs were observed. In addition, no gross or microscopic pathologic effects (including reproductive organs or nasal cavity changes) were observed. The mean body weights of exposed male rats were 4% to 12% higher throughout most of the study. Weight gains of exposed and control female rats were comparable. The mean body weight differences observed in exposed male rats were determined not to be related to treatment. The NOAEL for this study was 10,000 ppm.

B6C3F₁ mice (10/sex/group) were exposed by inhalation for 6 hours/day, 5 days/week for 14 weeks to 0; 625; 1,250; 2,500; 5,000; or 10,000 ppm propylene in air. Individual clinical observations were made daily. Body weights were recorded prior to exposure and at sacrifice (NTP, 1985). No treatment related deaths or clinical signs were observed. In addition, no gross or microscopic pathologic effects (including reproductive organs or nasal cavity changes) were observed. A 4% to 7% depression in final weight relative to the control weights occurred in female mice exposed to propylene for 14 weeks, but these differences were determined not to be treatment related. The NOAEL for this study was 10,000 ppm.

The two studies described above were used to set the exposure concentrations for 2-year carcinogenicity studies. These studies are also key to the discussions about repeated dose toxicity.

Groups of 50 F344/N rats of each sex were exposed to propylene in air (98.6% to 99.7% pure) by inhalation at concentrations of 5,000 or 10,000 ppm, 6 hours per day, 5 days per week, for 103 weeks. Other groups of 50 rats of each sex received air only on the same schedule and served as chamber controls. The highest concentration of propylene that was considered safe was 10,000 ppm because of the risk of explosion that can occur at higher concentrations. The survival of exposed and control rats was comparable. Throughout most of the studies, mean body weights of exposed male and female rats were slightly lower (0 to 5%) than those of the controls, but the decrements were not concentration related. No compound-related adverse clinical signs were observed. No gross or microscopic lesions of the reproductive organs were observed. Histopathological examinations revealed an increased incidence of squamous metaplasia at 5,000 and 10,000 ppm and inflammation of the nasal cavities at 10,000 ppm. Based on these findings the NOAEL is <5,000 ppm (detailed discussion in Section 3.7).

B6C3F₁ mice (50 males and 49 to 50 females/group) were exposed to propylene in air (98.6% to 99.7% pure) by inhalation at concentrations of 5,000 or 10,000 ppm, 6 hours per day, 5 days per week, for 103 weeks. Other groups of 50 mice of each sex received air only on the same schedule and served as chamber controls. The highest concentration of propylene that was considered safe was 10,000 because of the risk of explosion that can occur at higher concentrations. The survival of exposed and control mice was comparable. After week 59 of the study, mean body weights of 10,000 ppm male mice were usually slightly lower (5%) than those of the controls, whereas those in other exposed groups of male and female mice were generally comparable with those of the controls. No compound-related adverse clinical signs were observed. No gross or microscopic

lesions of the reproductive organs or nasal cavity were observed. The NOAEL for this study was 10,000 ppm.

The histopathological findings from the rat and mouse 2-year studies are discussed in detail in the carcinogenicity section (Section 3.7) below.

A repeated dose propylene biomarker/mutagenicity dose-response study was conducted using male F344 rats (8/group) exposed by inhalation to atmospheres containing 0; 200; 2,000; or 10,000 ppm propylene in air for 6 hours/day, for a total of 1, 3, or 20 exposures (5 days per week over 4 weeks) (DuPont, 2002a). While there were no substantial differences between males and females for most endpoints in previous studies, females did appear to be slightly more sensitive to nasal irritation. Therefore, the subgroup receiving 20 exposures followed by cell proliferation/histopathology analyses contained females as well as males. Sections of the nasal cavity of rats from all exposure groups were microscopically examined as were similar nasal tissue sections that were immunohistochemically prepared to identify nasal epithelial cells undergoing DNA synthesis with intranuclear incorporation of bromodeoxyuridine (BrdU). No propylene-specific nasal lesions were microscopically detected in any of the male or female exposed to 200; 2000; or 10,000 ppm for 3 or 20 days. No exposure-related inflammation (rhinitis) or alterations (e.g., degeneration, necrosis, hyperplasia, metaplasia) in the squamous, transitional, respiratory or olfactory epithelium lining the nasal airways were found in any of the sections examined from these propylene-exposed rats. In addition, there were no apparent exposure-related changes, compared to that of controls, in the density of BrdU-labelling in the four specific nasal epithelial populations. Furthermore, there were no test substance-related effects on cell proliferation in the liver or nasal respiratory epithelium for any exposure concentration. Under the conditions of the study, the NOAEL was 10,000 ppm (the highest concentration tested) in males and females.

Conclusion

These studies demonstrate that propylene produced no clinical effects in rodents exposed to concentrations up to 10,000 ppm, one-half of the lower flammability limit, for up to 14 weeks. However, based on the increased squamous metaplasia and inflammation of the nasal cavities in the rat observed during the 2-year inhalation studies, the chronic NOAEL is <5,000 ppm.

Table 9. Summary of Repeated Dose Toxicity Data for the Propylene Streams Category

CAS RN and Substance Name	Test Organism	Exposure Duration (weeks)	NOAEL (ppm)
115-07-1 Propylene	Rat	14	10,000
115-07-1 Propylene	Mouse	14	10,000
115-07-1 Propylene	Rat	103	<5,000
115-07-1 Propylene	Mouse	103	10,000

4.1.5 Mutagenicity

In vitro Studies

Propylene

An Ames assay, with and without metabolic activation, was conducted in *Salmonella typhimurium* strains TA1535, TA100, TA1537, TA98 and *Escherichia coli* strain WP2uvrA(pKM101). Propylene concentrations up to 10,000 ppm, approximately one-half the lower flammability limit

were tested (0, 0.031%, 0.063%, 0.125%, 0.25%, 0.5% and 1% propylene). The study showed some mutagenic activity at propylene concentrations $\geq 0.5\%$ (5,000 ppm) in TA1535 in the presence of S9 suggesting that propylene metabolites are positive in this one strain; all other *Salmonella* strains and *E. coli* were negative (Inveresk Research, 2003). Previous Ames assays in strains TA97 and TA98 (Hughes *et al.*, 1984) and TA100 (Victorin and Stahlberg, 1988; Kleindienst *et al.*, 1992) were also negative. A mouse lymphoma assay conducted at concentrations from 20-50% showed no evidence of mutagenicity in the absence of S9 but could not be classified as mutagenic or non-mutagenic in the presence of S9 (McGregor *et al.*, 1991).

Propane

An Ames assay was conducted with and without metabolic activation in 5 strains of *Salmonella typhimurium*, i.e., TA98, TA100, TA1535, TA1537, and TA1538 (Kirwin and Thomas, 1980). In this study plates were exposed in desiccators to 10, 20, 30, 40 and 50% propane in air. The plates were exposed to the gas mixtures for 6 hours in the sealed desiccators, after which they were removed and incubated at 37°C for an additional 40 to 45 hours. The number of histidine revertants were counted and recorded. Negative and positive controls were also carried out. In this study propane was neither toxic nor mutagenic at any of the concentrations tested either with or without metabolic activation

In vivo Studies

Propylene

Mouse Micronucleus Assay

Propylene was evaluated *in vivo* for its ability to induce micronuclei in bone marrow polychromatic erythrocytes (PCEs) in male Fischer 344 (F344) rats. Groups of 8 rats were exposed to 200, 2,000, and 10,000 ppm propylene, clean air by inhalation, or positive control substance by inhalation for 6 hours/day, 5 days/week, for a total of 20 exposures. The positive control substance (cyclophosphamide) was administered to untreated animals by ip injection from 24 to 48 hours prior to terminal sacrifice. Bone marrow smears were prepared immediately after sacrifice. No statistically significant test substance-related increases in the micronucleated PCE frequencies were observed in any dose group and no statistically significant test substance-related decreases in the proportion of PCEs among 1,000 erythrocytes were observed in any dose group. Under the conditions of this study, propylene did not induce any increase in micronucleated polychromatic erythrocytes in male rat bone marrow when evaluated after a total of 20 exposures. The highest exposure concentration, 10,000 ppm, was the NOEL. Therefore, the test substance was negative in this *in vivo* assay (DuPont, 2002b).

Hprt Assay

Walker *et al.* (2004) measured *Hprt* mutant frequencies in T-lymphocytes isolated and cultured from spleens of male F344 rats exposed to propylene at 200, 2,000, or 10,000 ppm for 20 days (6 hours/day for 5 days a week over 4 weeks), as well as negative (air only) and positive (cyclophosphamide) controls. All cloning efficiency plates and 6TG selection plates were blinded and designated by number assignments known only to appropriate contacts of the group. The scoring of all mutant lymphocytes was consistent throughout the study as demonstrated by periodic checks on the scoring of mutant lymphocytes. All mutation frequency calculations were reviewed and in agreement with study protocols. Appropriate statistical analyses were performed on raw data. Propylene did not produce an increase in *Hprt* mutant frequencies in splenic T-lymphocytes; the NOEL was 10,000 ppm (Walker *et al.*, 2004).

Conclusion

The overall weight of the experimental evidence indicate that propylene and propane are not likely to be weakly mutagenic in humans. Some mutagenic activity was observed with propylene in only one of five bacterial strains tested in the Ames assay (i.e., *Salmonella typhimurium* strain TA1535) in the presence of S9 suggesting that metabolites are weakly positive in this one strain. However, propylene was without activity in all other bacterial strains tested with and without metabolic activation. Moreover, a negative result was seen in an *in vitro* study in mouse lymphoma cells and in two well conducted *in vivo* mutagenicity studies. Two competent bioassays in rat and mouse conducted by the NTP are negative for carcinogenicity. Thus, propylene does not give any indication of being a genotoxic carcinogen.

4.1.6 Carcinogenicity

In vivo Studies in Animals

Groups of 50 F344/N rats of each sex were exposed to propylene (98.6% to 99.7% pure) in air by inhalation at concentrations of 5,000 or 10,000 ppm, 6 hours per day, 5 days per week, for 103 weeks (NTP, 1985). Other groups of 50 rats of each sex received air only on the same schedule and served as chamber controls. The highest concentration of propylene that was considered safe was 10,000 ppm because of the risk of explosion that can occur at higher concentrations.

The survival of exposed and control rats was comparable. Throughout most of the studies, mean body weights of exposed male and female rats were slightly lower (0 to 5%) than those of the controls, but the decrements were not concentration related. No compound-related adverse clinical signs were observed.

An increased incidence of squamous metaplasia of the nasal cavity was observed in female rats exposed at the 5,000 ppm and 10,000 ppm concentrations (control, 0/49; low, 15/50; high, 6/50) and in male rats exposed at 5,000 ppm (2/50; 19/50; 7/50). Epithelial hyperplasia of the nasal cavity was increased in female rats exposed at the 10,000 ppm concentration (0/49; 4/50; 9/50); the incidences in male rats were 2/50, 2/50, and 5/50. Inflammation of the nasal cavity, characterized by an influx of lymphocytes, macrophages, and granulocytes into the submucosa and by granulocytes into the lumen, occurred at increased incidences in low concentration and high concentration male rats and in high concentration female rats. No other effects were observed. However, these nasal cavity effects were not observed when rats were exposed to similar concentrations for 14 weeks in the range-finding study conducted to select the exposure concentrations for the carcinogenicity study (NTP, 1985). To further investigate this finding, a reevaluation of the archived tissue specimens from the NTP study was conducted (Harkema, 2002). The Harkema report is discussed in detail, below.

B6C3F₁ mice (50 males and 49-50 females/group) were exposed to propylene in air (98.6% to 99.7% pure) by inhalation at concentrations of 5,000 or 10,000 ppm, 6 hours per day, 5 days per week, for 103 weeks. Other groups of 50 mice of each sex received air only on the same schedule and served as chamber controls. The highest concentration of propylene that was considered safe was 10,000 because of the risk of explosion that can occur at higher concentrations.

The survival of exposed and control mice was comparable. After week 59 of the study, mean body weights of 10,000 ppm male mice were usually slightly lower (5%) than those of the controls, whereas those in other exposed groups of male and female mice were generally comparable with those of the controls. No compound-related adverse clinical signs were observed.

Upon histological examination, chronic focal inflammation of the kidneys was observed at an increased incidence in both low and high concentration mice of each sex. However, a reevaluation of archived specimens showed no evidence of renal tubule injury as indicated by an absence of any apparent increase in cytoplasmic vacuolation, cell degeneration / death, apoptosis or necrosis,

mitotic activity, or tubule hyperplasia compared to the control animals. Chronic progressive nephropathy affected over 85% of mice in each group, but at low grades of severity. The mode for grade of severity was 1, or minimal, in each group with no difference between groups (Hard, 2001).

Hemangiosarcomas were found in one low dose male mouse (liver), two high dose male mice (spleen) and three high dose female mice (subcutis, spleen, and uterus). Haemangiomas were found in one low dose and in one high dose female mouse (liver). Vascular tumors were not found in control mice of either sex. The incidences of vascular tumors and their occurrence in a variety of organs suggest that they are not related to administration of propylene.

The occurrence of uterine endometrial stromal polyps in female mice showed a positive trend ($P < 0.05$; 0/47; 0/47; 3/48); the incidence in the 10,000 ppm group was not significantly greater than that in the concurrent control group, but the incidence was higher than the mean historical control rate (22/ 2,411, 0.9%) and was within the range (0% to 6%) observed in studies throughout the Carcinogenesis Program. The occurrence of endometrial stromal polyps in three high concentration female mice was not considered to be clearly related to exposure to propylene.

The incidence of male mice with alveolar/bronchiolar adenomas or carcinomas (combined) occurred with a negative trend ($P < 0.05$; 16/50; 4/49; 7/50), and the reduced incidences in both exposed groups were less ($P < 0.05$) than that in the control group. The control incidence of these tumours in an inhalation study conducted concurrently at the same laboratory was similar (15/50), suggesting a possible exposure-related decrease. The biologic significance of this decrease in male mice is difficult to assess; the incidences seen in these control and exposed animals are within the range of incidences (2% to 34%; mean, 16.7%) observed in control male mice in other studies throughout the Carcinogenesis Program.

The nasal cavity findings in the NTP studies were further evaluated by Harkema (2002). An increased incidence of nasal inflammation (rhinitis) in male and female rats chronically exposed to 5,000 or 10,000 ppm propylene compared to filtered-air control rats (0 ppm propylene) was noted by both Harkema and the NTP. Harkema (2002) also found a slightly higher incidence of rhinitis in female mice exposed to 5,000 or 10,000 ppm propylene compared to control mice. There was also a slight increase in the incidence of nasal inflammation in the low-dose exposed, but not the high-dose exposed male mice compared to control male mice. In addition, Harkema cited some additional exposure-related epithelial alterations that were not identified in the NTP report. These included mucous cell hyperplasia in nasal respiratory epithelium of propylene-exposed male and female rats, and a propylene-related increase in the amount of eosinophilic globules in olfactory epithelium in male and female rats (both low and high doses) and female mice exposed to the low dose. Both of these epithelial alterations are thought to be common non-specific responses of the airway epithelium to inhaled irritants. These changes in the surface epithelium probably reflect secretory defense mechanisms of the airways to prevent further damage from the inhaled irritant (e.g., mucous cell hyperplasia suggests an increased production, storage and secretion of airway mucus).

Other than a higher incidence of squamous metaplasia in low-dose female rats compared to high-dose exposed female rats, the incidence of propylene-induced nasal lesions were very similar suggesting that a threshold in response occurred in female rats at 5,000 ppm. Interestingly, male rats exposed to the low dose of propylene had a higher incidence of most of the nasal lesions (i.e., squamous metaplasia, mucous cell metaplasia, eosinophilic hyalinosis) than the rats exposed to the high dose. However the incidence of male rats with propylene-induced epithelial hyperplasia was significantly greater in those exposed to 10,000 ppm compared to those exposed to 5,000 ppm.

There was no apparent direct dose-response relationship in rats or mice. The incidences of most of the nasal lesions (with the exception of epithelial hyperplasia) in male rats were more common in those chronically exposed to the low rather than the high dose of propylene. Likewise, male mice exposed to the low dose of propylene had a higher incidence of rhinitis than those male mice

exposed to the high dose. In addition, the increased incidence of rhinitis in female rodents (rats and mice) was similar after low- or high-dose exposure to propylene.

Comparing the non-neoplastic lesions of male and female rats (and mice) exposed to the high-dose of propylene, the incidence and the severity of the lesions appeared to be slightly greater in the female animals suggesting a modest gender-related difference. Gender-related differences in response to inhaled agents are not uncommon. The specific biological reasons for these differences could not be determined in the present study.

In conclusion, the nasal histopathology of both the rats and mice exposed by chronic inhalation to propylene (5,000 or 10,000 ppm) indicates that this chemical agent induces mild rhinitis (nasal inflammation) and associated epithelial alterations suggesting chronic, low-grade irritation in these rodents. However, there was no obvious dose-response relationship in either the rats or mice. This may suggest a possible threshold effect at the low dose (5,000 ppm) for most of the observed nasal lesions. There was also a modest gender effect with female rodents (rats and mice) having a slightly higher incidence of propylene-induced nasal lesions compared to similarly exposed males. In addition, rats had more exposure-related nasal epithelial alterations than did the similarly exposed mice (Harkema, 2002).

The recent repeated dose inhalation study indicated no propylene-specific nasal lesions were microscopically detected in any of the male or female rats exposed to 200; 2,000; or 10,000 ppm for 3 or 20 days. There was no exposure-related inflammation (rhinitis) or alterations (e.g., degeneration, necrosis, hyperplasia, metaplasia) in the squamous, transitional, respiratory or olfactory epithelium lining the nasal airways in any of the sections examined from these propylene-exposed rats. In addition, there were no apparent exposure-related changes, compared to that of controls, in the density of BrdU-labelling in the four specific nasal epithelial populations (DuPont, 2002a).

Conclusion

Under the conditions of these studies, there was no evidence of carcinogenicity in male and female F344/N rats or in male and female B6C3F1 mice exposed to propylene by inhalation at concentrations of 5,000 or 10,000 ppm for 103 weeks. In the nasal cavity, propylene induced squamous metaplasia of the respiratory epithelium in male and female rats and epithelial hyperplasia in female rats; however, recent re-evaluation of this study and new data indicate there is no dose-response. The NOEL for carcinogenicity was 10,000 ppm.

4.1.7 Toxicity for Reproduction

Reproductive and Developmental Toxicity

Studies in Animals

Propylene

A prenatal developmental inhalation toxicity study conducted to OECD TG 412/414 under GLP was selected as the critical study (BASF, 2002). Twenty-five female Wistar rats per test group were whole-body exposed to dynamic atmospheres of propylene for 6 hours per day on day 6 through day 19 *post coitum* (p.c.) for a total of 14 exposures. The target concentrations were 200; 1,000; and 10,000 ppm. A concurrent control group was exposed to clean air. Chamber concentrations were determined analytically using a gas chromatographic method.

The general state of health was examined twice each day. On exposure days, clinical observations were performed before, during, and after exposures. During the acclimation period and on post exposure days clinical findings were recorded once each working day. Food consumption, water consumption, and body weight of the animals were each determined three or four times per week during the study.

On day 20 post coitum, all animals were sacrificed and assessed by gross pathology (including weight determinations of the unopened uterus and the placentae). For each dam, corpora lutea were counted and number and distribution of implantation sites (differentiated as resorptions, live and dead fetuses) were determined. The fetuses were removed from the uterus, sexed, weighed and further investigated for any external findings. Thereafter, about one half of the fetuses of each litter were examined for soft tissue findings and the remaining fetuses for skeletal (including cartilage) findings. There were no substance-related effects on the dams concerning food and water consumption, body weight, body weight change, uterine weights, corrected body weight change, or clinical and necropsy observations up to and including a concentration of 10,000 ppm.

There were no differences of toxicological relevance between the control and the substance exposed groups (200; 1,000; and 10,000 ppm) on the gestational parameters, i.e., in conception rate, mean number of corpora lutea, total implantations, resorptions and live fetuses, fetal sex ratio or in the values calculated for the pre- and the post-implantation losses. No substance-related differences were recorded for placental and fetal body weights. The external, soft tissue and/or skeletal examinations of the fetuses revealed no toxicologically relevant differences between the control and the substance-exposed groups.

Reproductive organs (i.e., mammary gland, seminal vesicles, prostate, testes, ovaries, uterus) from the NTP repeated dose studies described above, were subjected to histopathologic evaluation. There were no exposure related, statistically significant findings in any tissue examined. Uterine endometrial stromal polyps were observed in all exposure groups of rats and in the high exposure group mice in the 104 week study. There was no difference between exposure groups in rats (2/46, 7% in controls; 4/47, 9% low exposure; 4/49, 8% in high exposure animals). This finding was not observed in control or low exposure group mice. The incidence in the high exposure group mice (3/48, 6%) was within the range of historic controls and thus was not considered to be clearly associated with exposure to propylene.

Conclusion

Under the conditions of the study, the inhalation exposure of pregnant Wistar rats to propylene from implantation to one day prior to the expected day of parturition (days 6 to 19 p.c.) elicited no maternal toxicity, prenatal or developmental toxicity, or teratogenicity at all tested concentrations up to 10,000 ppm (Table 10). The highest dose, 10,000 ppm, is in the range of the lower explosive limit.

These findings, along with the findings of no biologically significant effects on male or female reproductive organs attributed to propylene exposure in repeated dose inhalation studies in two species, leads to a conclusion of low concern for reproductive toxicity.

Table 10. Summary of Developmental Toxicity Data for the Propylene Streams Category

CAS RN and Substance Name	Test Organism	OECD Test Guideline	NOEL (ppm)
115-07-1 Propylene	Rat	412 / 414	10,000

4.2 Assessment Summary for Human Health

Propylene and propane have a low order of acute toxicity. As they are both gases at normal temperature and pressure, ingestion or dermal absorption of these materials is unlikely. Inhalation of propylene and propane can produce narcosis and anaesthesia. However, these effects are only seen at very high concentrations (>46,000 ppm to induce narcosis in humans).

In the gaseous state propylene and propane are not irritating to the skin or eyes. However, should skin or eye contact occur to either of these chemicals in their liquid state, tissue freezing, severe cold burn, and/or frostbite may result.

No clinical effects were observed in 14 week and 103 week repeated dose toxicity studies using rats and mice, up to an exposure level of 10,000 ppm. Furthermore, there was no evidence of carcinogenicity in rats and mice exposed to propylene concentrations as high as 10,000 ppm for 103 weeks. Inflammation of the nasal cavity was the only indication of toxicity observed following exposure of male rats to 5,000 and 10,000 ppm propylene and female rats exposed to 10,000 propylene for 103 weeks. These effects were not observed when rats were exposed to similar concentrations for 14 weeks. To further investigate this finding, a recent repeated dose inhalation study indicated no propylene-specific nasal lesions were microscopically detected in any of the male or female rats exposed to 200; 2000; or 10,000 ppm for 3 or 20 days. No exposure-related inflammation (rhinitis) or alterations (e.g., degeneration, necrosis, hyperplasia, metaplasia) in the squamous, transitional, respiratory, or olfactory epithelium lining the nasal airways were found in any of the sections examined from these propylene-exposed rats. In addition, there were no apparent exposure-related changes, compared to that of controls, in the density of BrdU-labelling in the four specific nasal epithelial populations. These studies demonstrate that propylene produced no clinical effects in rodents exposed to concentrations up to 10,000 ppm, one-half of the lower flammability limit, for up to 14 weeks. However, based on the 103-week repeated dose study in which increased squamous metaplasia and inflammation of the nasal cavities were observed in rats the NOEL is <5,000 ppm.

Propane was negative for mutagenicity when tested in the *in vitro* Ames assay in five strains of *Salmonella typhimurium*. Propylene induced weak mutagenic activity in only one test strain when tested in the *in vitro* Ames *Salmonella* mutagenicity assay at concentrations $\geq 0.5\%$ (5,000 ppm). However, propylene was negative in other Ames assays and in the *in vitro* mouse lymphoma assay. In addition, propylene was negative in two well conducted *in vivo* mutagenicity studies. The NOEL for *in vivo* mutagenicity is 10,000 ppm.

A prenatal developmental inhalation exposure elicited no maternal toxicity, prenatal, or developmental toxicity, or teratogenicity at propylene concentrations up to 10,000 ppm, the NOEL in this study.

5 HAZARDS TO THE ENVIRONMENT

5.1 Aquatic Toxicity

The aquatic toxicity of streams in this category is expected to fall within a relatively narrow range regardless of their composition. This is expected, because the constituent chemicals of these streams are neutral organic hydrocarbons whose toxic mode of action is non-polar narcosis (Ramos *et al.*, 1998). The toxic mechanism of short-term toxicity for these chemicals is disruption of biological membrane function (Van Wezel, 1995), and the differences between toxicities (i.e., LC/LL₅₀, EC/EL₅₀) can be explained by the differences between the target tissue-partitioning behavior of individual constituent chemicals (Verbruggen *et al.*, 2000).

The existing fish toxicity database for hydrophobic, neutral organic chemicals, which compose the streams in this category, supports a critical body residue (CBR) for these chemicals between approximately 2 to 8 mmol/kg fish (wet weight) (McCarty *et al.*, 1991; McCarty and Mackay, 1993). The CBR is the internal concentration of a toxicant that causes mortality. When normalized to lipid content for most organisms, the CBR is approximately 50 $\mu\text{mol/g}$ of lipid (Di Toro, 2000). Therefore, only hydrocarbon streams with components of sufficient water solubility, such that their

molar sum in solution is high enough to produce a total partitioning to the organism of approximately 50 μmol of hydrocarbon per gram of lipid will demonstrate lethality.

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

Calculated aquatic toxicity values for chemicals representative of category members fall within a relatively narrow range. The effect range is a function of the range of $\log P_{ow}$ values identified for the chemicals. Streams in this category are expected to demonstrate 96-hour LC_{50} fish toxicity values in the range of 15.0 to 97.7 mg/L, 48-hour EC_{50} invertebrate toxicity values in the range of 16.5 to 100.8 mg/L, and 96-hour EC_{50} alga toxicity values in the range of 10.5 to 61.0 mg/L (Table 12).

Table 11. Summary of Calculated Aquatic Toxicity Data for Chemical Constituents in the Propylene Streams Category

Chemical Constituent (Log P_{ow}*)	Fish Toxicity 96-hour LC_{50} (mg/L)	Invertebrate Toxicity 48-hour EC_{50} (mg/L)	Alga Toxicity 96-hour EC_{50} (mg/L)
Propadiene (1.45)	97.7	100.8	61.0
Propylene (1.77)	51.3	54.1	33.4
Propane (2.36)	15.0	16.5	10.5

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

5.2 Assessment Summary for the Environment

Results of distribution modeling show that streams in the Propylene Streams Category will partition primarily to the air compartment, with a negligible amount partitioning to water. Although constituents have a moderate degree of water solubility, wet deposition of category constituents is not likely to play a significant role in their atmospheric fate because they rapidly photodegrade. Volatilization to the air will contribute to the rapid loss of category constituents from aqueous and terrestrial habitats. In the air, these constituents have the potential to rapidly degrade through indirect photolytic processes mediated primarily by hydroxyl radicals with calculated degradation half-lives ranging from 4.9 to 101.2 hours, depending on hydroxyl radical concentration. Aqueous photolysis and hydrolysis will not contribute to the transformation of category constituents in aquatic environments because they are either poorly or not susceptible to these reactions.

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

Due to the fact that streams in this category are gaseous at ambient temperature and pressure and expected to partition predominantly to the atmosphere, no aquatic toxicity testing was conducted. However, the ECOSAR model was used to predict aquatic toxicity using the equation for neutral organics, a reliable estimation method for this class of chemicals. Calculated acute toxicity values of selected category constituents for fish (96-hr) and invertebrates (48-hr) range from 15.0 to 97.7 mg/L and from 16.5 to 100.8 mg/L, respectively. For algae, the calculated 96-hr EC₅₀ ranges from 10.5 to 61.0 mg/L.

6 DATA SUMMARY

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

- **Propylene, Polymer Grade**
 - 115-07-1
- **Propylene, Chemical Grade**
 - 115-07-1
- **Propylene Stream**
 - A mixture of 115-07-1, 74-84-0 and 74-98-6
 - 68606-26-8
- **Light Ends from Butadiene Plant**
 - 68606-26-8

Table 12. Physico-Chemical and Environmental Data Used to Characterize Streams and CAS RNs in the Propylene Streams Category (ranges are based on data for the most representative chemical subset for category streams and CAS RNs)

Endpoint	Propylene Streams Category Streams and CAS RNs			
	Propylene, Polymer Grade	Propylene, Chemical Grade	Propylene Stream	Light Ends from Butadiene Plant
	115-07-1	115-07-1	Mixture of 115-07-1, 74-84-0, 74-98-6, and 68606-26-8	68606-26-8
Melting Point*/ Range (°C)	-187.6 to -136.2 (m)			
Boiling Point*/ Range (°C)	-47.6 to -34.4 (m)			
Vapor Pressure*/ Range (hPa)	7.24 E3 to 1.16 E4 (m)			
Log P _{ow} */ Range	1.45 to 2.36 (m)			
Water Solubility*/ Range (mg/L)	200 to 2,147 (m)			
Direct Photodegradation	Direct photolysis will not contribute to degradation			
Indirect (OH-) Photodegradation* (half-life, hrs) (c)	4.9 to 101.2 (a)			
Hydrolysis	Hydrolysis will not contribute to degradation			
Distribution*	>99.4% partitions to air <0.5% partitions to water			
Biodegradation	Potential to biodegrade			
96-hr Fish Acute Toxicity* (mg/L)	15.0 to 97.7 (c)			
48-hr Daphnid Acute Toxicity* (mg/L)	16.5 to 100.8 (c)			
96-hr Alga Toxicity* (mg/L)	10.5 to 61.0 (c)			

* Constituent chemicals used to define selected endpoints include: propadiene, propylene, and propane

(m) Measured values

(c) Calculated values

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

Table 13. Human Health Data Summary Used to Characterize Streams and CAS RNs in the Propylene Streams Category

Endpoint	Human Health Data for Propylene Streams Category Streams (CAS RNs)			
	Propylene, Polymer Grade	Propylene, Chemical Grade	Propylene Stream	Light Ends from Butadiene Plant
	115-07-1	115-07-1	Mixture of 115-07-1, 74-84-0, 74-98-6, and 68606-26-8	68606-26-8
Acute Toxicity (rat)	LC50 >65,000 ppm			
Irritation	Little to None (eyes / skin)			
Repeat Dose Toxicity	NOEL = 10,000 ppm; 70-day exposure (rat, mouse) NOEL = 10,000 ppm; 515-day exposure (mouse) NOEL <5,000 ppm; 515-day exposure (rat)			
Mutagenicity <i>in vitro</i>	Negative			
Mutagenicity <i>in vivo</i>	Negative			
Carcinogenicity (rat, mouse)	Negative (NOEL = 10,000 ppm)			
Reproductive Toxicity (rat)	NOEL = 10,000 ppm			
Developmental Toxicity (rat)	NOEL = 10,000 ppm			

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APPENDIX I**ETHYLENE PROCESS DESCRIPTION****A. Ethylene Process (including propylene)****1. Steam Cracking**

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

Subjecting the feedstocks to high temperatures results in the partial conversion of the feedstock to olefins. In the simplest example, feedstock ethane is partially converted to ethylene and hydrogen. Similarly, propane, butane, or the liquid feedstocks are also converted to ethylene. While the predominant products produced are ethylene and propylene, a wide range of additional products are also formed. These products range from methane (C1) through fuel oil (C12 and higher) and include other olefins, diolefins, aromatics and saturates (naphthenes and paraffins).

2. Refinery Gas Separation

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

B. Products of the Ethylene Process

The intermediate stream that exits the cracking furnaces (i.e., the furnace effluent) is forwarded to the finishing section of the ethylene plant. The furnace effluent is commonly referred to as “cracked gas” and consists of a mixture of hydrogen, methane, and various hydrocarbon compounds with two or more carbon atoms per molecule (C2+). The relative amount of each component in the cracked gas varies depending on what feedstocks are cracked and cracking process variables. Cracked gas may also contain relatively small concentrations of organic sulfur compounds that were present in the feedstock or were added to the feedstock to control coke formation. The cracked gas stream is cooled, compressed and then separated into the individual streams of the ethylene process. These streams can be sold commercially and/or put into further steps of the process to produce additional materials. In some ethylene processes, a liquid fuel oil product is produced when the cracked gas is initially cooled. The ethylene process is a closed process and the products are contained in pressurized systems.

The final products of the ethylene process include hydrogen, methane (frequently used as fuel), and the high purity products ethylene and propylene. Other products of the ethylene process are typically mixed streams that are isolated by distillation according to boiling point ranges and then further processed. Product propylene and propylene streams from the ethylene unit and from down

stream processing make up the Propylene Streams Category. Categories sponsored by the Olefins Panel of the American Chemistry Council are listed in Table 14.

The chemical process operations that are associated with the process streams in the Propylene Streams Category are shown in Figure 5.

Figure 5. Propylene Streams Process Streams Flow Diagram from the Ethylene Manufacturing Process Unit

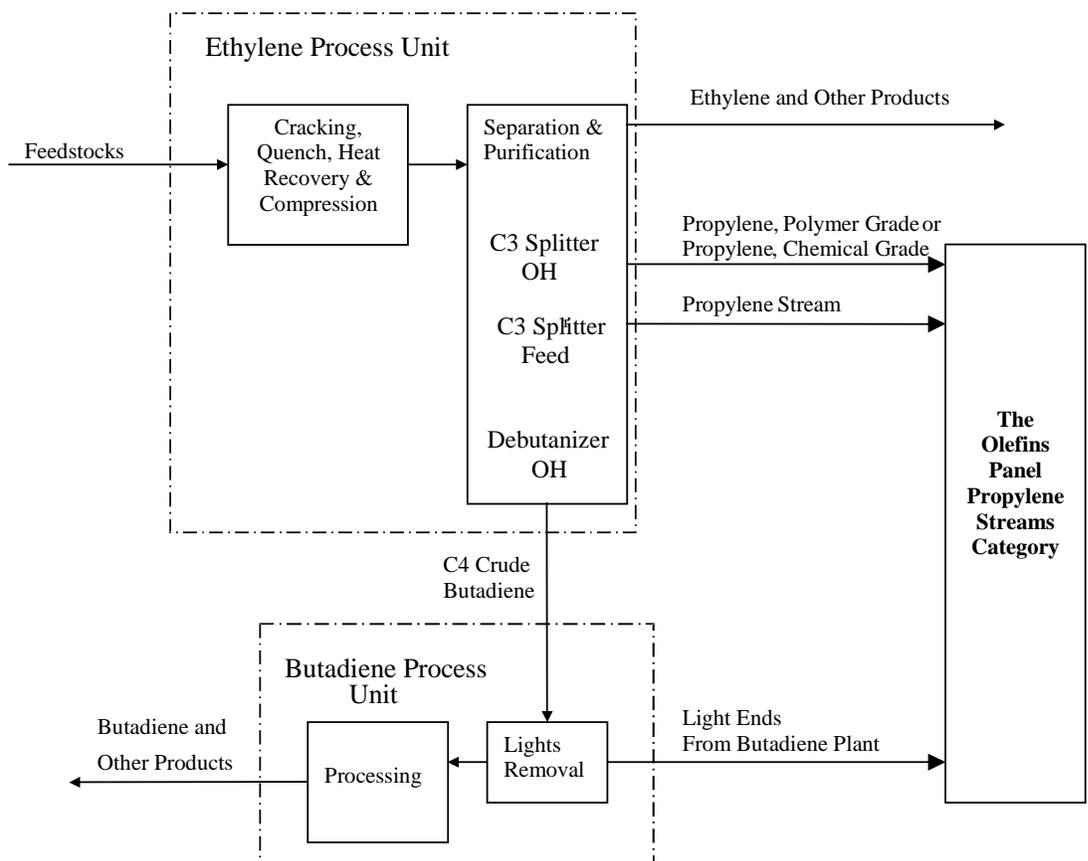


Table 14. HPV Program Categories Sponsored by the Olefins Panel of the American Chemistry Council

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