U.S. EPA HPV Challenge Program

Hazard Characterization for

Distillates (petroleum), steam-cracked petroleum distillates, C5-18 fraction

CAS Number 68477-58-7

Submitted by the American Petroleum Institute
Petroleum HPV Testing Group
Consortium Registration #1100997

American Petroleum Institute
1220 L Street NW
Washington, DC 20005

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Summary

Distillates (petroleum), steam-cracked petroleum distillates, C5-18 fraction (hereafter called steam-cracked distillates) has the Chemical Abstract Services (CAS) number 68477-58-7 and the following CAS definition, *A complex combination of organic compounds obtained by the multiple distillation of steam-cracked distillates to which hydrocarbons having carbon numbers predominantly in the range of C5 through C12 from distillation of polymerized steam-cracked distillates may have been added. It consists of hydrocarbons having carbon numbers predominantly in the range of C5 through C18.*

This substance spans the carbon number and boiling range of substances found in the Petroleum HPV Categories; Gasoline Blending Streams and Kerosene/Jet Fuel. Therefore the range of physical/chemical properties, environmental fate, and environmental effects for steam-cracked distillates can often be predicted from data in those previously submitted categories. This substance is also compositionally similar to the Type I aromatic naphthas defined by ASTM D 3734, *Standard Specification for High-Flash Aromatic Naphthas* (ASTM International, 2011). That solvent is represented by the substance, Solvent naphtha (petroleum), light aromatics - CAS number 64742-95-6, more commonly called C9 Aromatics.

Two manufacturers reported producing steam-cracked distillate in 2006, however only one manufacturer is still isolating this substance and therefore only one sample was available for analytical characterization. The substance is normally consumed on-site in the manufacturer of petroleum resins. The measured distillation range of the supplied sample was 67 *°C to 220 °C (152 °F to 428 °F*).

Based on the carbon range of C5 to C18, freezing points of less than -40*°C* would be expected. The physical-chemical characteristics of the steam-cracked distillates also include an estimated range of vapor pressures between 10 hPa to 9150 hPa, indicating a tendency to volatilize. For constituent hydrocarbons in steam-cracked distillates, partition coefficients are expected to range from 1.23 to >6, while water solubility values are expected to range from <1 mg/l to 2000 mg/L.

If released into the environment, individual components of steam-cracked distillates will disperse and partition according to their individual physical-chemical properties. The final dispositions of these components are shaped by both abiotic and biotic processes. Based on modeling of individual chemical encompassing the different types and molecular weights of hydrocarbons making up steam-cracked distillates, volatilization to the atmosphere is predicted to be an important distribution process. Residence times in the atmosphere are expected to be relatively short due to indirect photodegradation reactions. In water, hydrolysis is not likely to occur, as the chemical linkages of hydrocarbons do not allow for these reactions. However, biodegradation data show that gasoline blending streams and substances in the kerosene category can exhibit a moderate to rapid rate of biodegradation and are considered at least inherently biodegradable.

Based on the studies identified to represent the acute toxicity of gasoline blending streams to aquatic organisms, the proposed “read-across” ranges of acute toxicity for steam-cracked distillates (expressed as lethal loading rates) are 2.09 to 46 mg/L, 0.9 to 32 mg/L, and 1.1 to 64 mg/L (fish, invertebrates, and algae respectively). The substances in the Kerosene/Jet Fuel Category produce a similar (but narrower) range of toxicity values for the same aquatic species when studies using similar solution preparation and exposure techniques were compared. A commercial C9 Aromatic solvent was tested in fish and invertebrates for acute toxicity with water accommodated fractions and gave EC50 results of 9.22 mg/l (96-hr) and 6.14 mg/l (48-hr) respectively.

Because of the carbon number range found in steam-cracked distillates, both inhalation and dermal routes of exposure are considered relevant in assessing the potential for human health hazards. Data on gasoline blending streams and C9 Aromatics are used to estimate inhalation hazards and data on kerosene/jet fuel category members are used to estimate dermal hazards.

Results of testing on gasoline blending streams, kerosene/jet fuel category members and a commercial C9 Aromatic solvent for acute toxicity lead to predictions that steam-cracked distillates would demonstrate consistently low toxicity by the oral [Rat LD50 >5g/kg], dermal [Rabbit LD50 >2g/kg] and inhalation [Rat LC50 >5g/m^3] exposure routes. “Steam-cracked distillates” is expected to be a mild to moderate eye and skin irritant. No skin sensitization potential is anticipated.

C9 Aromatics were evaluated for neurotoxicity after a 13-week repeat dose inhalation exposure (6hr/d, 5d/w) at concentrations of 101, 452, and 1320 ppm. In this study, other than a transient weight reduction in the high exposure group (not statistically significant at termination of exposures) No effects were noted on startle response, forelimb and hind limb grip strength, hind limb splay, or thermal response. No effects were noted on motor activity at any treatment level. Examination of sections of brain, cervical and lumbar spinal cord, and left and right proximal sciatic nerves failed to reveal any neurotoxic change.The read-across value for inhalation of steam-cracked distillates is NOAEC = 1320 ppm.

The potential *in vitro* genotoxicity of gasoline blending streams and kerosene/jet fuel materials has been evaluated in a variety of studies. Standard Ames assays, optimized Ames assays, mouse lymphoma assays, and sister chromatid exchange assays have been conducted with predominately negative results. For C9 Aromatics, in vitro genotoxicity studies included the *Salmonella*/mammalian microsome mutagenicity assay, the hypoxanthine-guanine phosphoribosyl transferase (HGPRT) forward mutation assay in CHO cells, and *in vitro* chromosome aberration and sister chromatid exchange (SCE) assays in CHO cells. There was no evidence that C9 Aromatics was either a gene or chromosomal mutagen. The read-across conclusion for steam-cracked distillates is that it will not be genotoxic under *in vitro* conditions.

Many *in vivo* genotoxicity studies have been done on a variety of gasoline blending streams and kerosene/jet fuel materials. Bone marrow cytogenetic tests, sister chromatid exchange assays, dominant lethal assays, and red blood cell micronucleus studies have been conducted with predominately negative results. An *in vivo* chromosome aberration assay in rat bone marrow was done on C9 Aromatics and was negative. The read-across conclusion for steam-cracked distillates is that it will not be genotoxic under *in vivo* conditions.

C9 Aromatics were tested for developmental toxicity in CD-1 mice by inhalation exposure to concentrations of 100, 500, or 1500 ppm. Developmental toxicity was observed at the 500 and 1500 ppm dose levels. This was manifested as a significant increase in mean postimplantation loss at 1500 ppm, and significant decreases in mean fetal body weights at 500 and 1500 ppm levels. It should be noted, however, that there was evidence of severe maternal toxicity at 1500 ppm and that maternal weight gain was reduced at 500 ppm.

C9 Aromatics were also testing for reproductive toxicity in SD rats by inhalation exposure to concentrations of 103, 495 1480 ppm in a three generation reproductive study. Animals in the F0,F1, and F2 generations were exposed for 10 weeks prior to mating. Mortality in the F1, F2, and F3 generations was observed in the 1480 ppm treated groups. The LOAEC with respect to F0 and F1 parental systemic toxicity was 495 ppm, based on reduced body weights observed in the F2 generation. The developmental LOAEC was determined to be 495 ppm based on reduced body weight in the F3 pups; maternal body weight was also reduced in the 495 ppm treated group. No reproductive effects were observed at the highest dose tested. However, a full evaluation of the 1480 ppm F2 generation was precluded due to excessive mortality (only six dams available); no reproductive effects were observed in these dams. The read-across ranges for inhalation of steam-cracked distillates are:

Developmental NOAEC = 100 ppm (Mice)
Reproductive NOAEC = 495 ppm (Rat) which excludes analysis of the highest concentration due to excessive mortality.

Introduction

Distillates (petroleum), steam-cracked petroleum distillates, C5-18 fraction (hereafter called steam-cracked distillates) has the Chemical Abstract Services (CAS) number 68477-58-7 and the following CAS definition, *A complex combination of organic compounds obtained by the multiple distillation of steam-cracked distillates to which hydrocarbons having carbon numbers predominantly in the range of C5 through C12 from distillation of polymerized steam-cracked distillates may have been added. It consists of hydrocarbons having carbon numbers predominantly in the range of C5 through C18.* Two facilities in the USA reported manufacturing steam-cracked distillates in 2006 (EPA, 2006).

Composition of Steam-cracked Distillates

A sample of steam-cracked distillate was analyzed for the endpoints that characterized High-Flash Aromatic Naphtha (ASTM D 3734). Table 1 compares the specification for ASTM D 37234 Type I solvents with a sample of steam-cracked distillate provided by a member company of the Petroleum HPV Testing Group (Sample 51:1).

Table 1. Comparison of Steam-cracked Distillates (Sample 51:1) with the Specification for High-Flash Aromatic Naphtha Type I (ASTM 3724)

Selected ASTM D 3734 Specifications	Method	Type I Specification	Sample 51:1
Aromatics, volume %, min	D 1319	90	83[a]
Corrosion, copper, 1/2 hour at 100C	D 849	Pass	Pass
Distillation, F	D 86		
Initial BP, min		300	152
5% recovered		-	303
50% recovered, max		335	324
95% recovered		-	425
Dry point, max		355	428
Flash point, F, min	D 56	100	87
Kauri-butanol value, min	D 1133	87	90
Mixed aniline point, max	D 611	60	72
Apparent specific gravity, 60/60F	D 4052		0.888
min		0.865	
max		0.882	

[a]The olefins and saturates content of Sample 51:1 was 12 and 5 percent respectively when measured by ASTM 1319.

The detailed composition of the aromatics in Sample 51:1 is shown in Table 2 in comparison to samples of C9 aromatic solvents.

Table 2. Comparison of Steam-cracked Distillates (Sample 51:1) with previously published examples of C9-Aromatics.

Test Material	Sample 51:1 CAS 68477-58-7	EPA C9 Test Rule CAS 64742-95-6	Clark et al., 1989 CAS 64742-95-6
Method	**ASTM D 5765**	**GC**	**GC**
Units	**wt%**	**wt%**	**% (m/m)**
Benzene	0.02		
Toluene	0.46		
Ethylbenzene	4.16		
M,P- Xylene	7.94		
1,2-Dimethylbenzene	5.06	3.2	2.27
Isopropyl-Benzene	1.14	2.74	
Propyl-Benzene	6.02	3.97	4.05
1-Methyl-3-Ethylbenzene	8.15	15.1	7.14
1-Methyl-4-Ethylbenzene	3.83	7.05	16.6
1,3,5-Trimethylbenzene	2.85	8.37	9.35
1-Methyl-2-Ethylbenzene	3.1	5.44	7.22

1,2,4-Trimethylbenzene	6.76	40.5	32.7
1,2,3-Trimethylbenzene	1.52	6.18	2.76
>C10s		6.19	
Indan	3.13		
Alkyl Indans	3.08		
1,4-Diethyl+Butylbenzene	1.3		
1,2-Diethylbenzene	0.06		6.54
1-Ethyl-3,5-dimethylbenzene			1.77
1,2,4,5-Tetramethylbenzene	0.1		
1,2,3,5-Tetramethylbenzene	0.14		
C10 Benzenes	1.37		
C11 Benzenes	0.24		
C12 Benzenes	<0.1		
Naphthalene	1.4		
2-Methyl-Naphthalene	0.06		
1-Methyl-Naphthalene	0.03		

Rationale for Predicting the Range of SIDS Endpoints

The CAS definition of steam-cracked distillates has a carbon range and boiling range that spans the existing Petroleum HPV Categories for Gasoline Blending Streams (C_4 to C_{12}) and Kerosene/Jet Fuel (C_9 to C_{16}). Therefore the range of physical & chemical properties, environmental fate, environmental effects and human health effects for steam-cracked distillates can be bounded by the Gasoline Blending Streams Category or the Kerosene/Jet Fuel Category. A supporting chemical with similar compositional characteristics, Solvent naphtha (petroleum), light aromatics (CAS 64742-95-6) also provides relevant information. Both inhalation and dermal routes of exposure are considered realistic.

The Category Assessment Document and Robust Summaries for Gasoline Blending Streams can be found at http://www.petroleumhpv.org/pages/gasoline.html and is referenced in this document as Petroleum HPV, 2008.

The Category Assessment Document and Robust Summaries for Kerosene/Jet Fuel can be found at http://www.petroleumhpv.org/pages/kerosene_jet.html and is referenced in this document as Petroleum HPV, 2010.

The IUCLID dossier for Solvent naphtha (petroleum), light aromatic (CAS 64742-95-6) from February 2000 is attached as Appendix 1.

Physical Chemical Properties

The physicochemical endpoints for the EPA HPV chemical program include melting point, boiling point, vapor pressure, octanol/water partition coefficient (log Kow), and water solubility.

Because of the complex nature of this substance, some physical-chemical properties are best represented by a range of values depending on the specific constituents and their concentrations in the various substances. For example, a complex substance containing a number of individual chemical constituents does not have a single boiling point, but a range of boiling points reflecting the constituent properties. Therefore, measured data were provided when available, calculations based on representative constituents were made when necessary, and technical discussions were given in those situations which do not apply to steam-cracked distillates.

For the physical-chemical properties that cannot be defined for complex substances, ranges of endpoint values were reported for representative paraffinic, naphthenic, olefinic, and aromatic hydrocarbons compounds (PONA) covering the relevant carbon range (C_5 to C_{18} carbon atoms). The EPI-Suite™ computer model (EPA, 2000), as discussed in the US EPA document entitled "The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program" (EPA, 1999) was used to calculate physical-chemical properties of representative hydrocarbon constituents.

Melting Point

For complex substances like petroleum products, there is no single melting point; rather, melting occurs over a range of temperatures reflecting the melting points of the individual components. To better describe the physical phase or flow characteristics of petroleum products, the pour point is routinely used. The pour point is the lowest temperature at which movement of the test specimen is observed under prescribed conditions of the test (ASTM, 1999). The substance's viscosity decreases as the pour point temperature falls. Kerosene range hydrocarbons have higher pour points than do gasoline range hydrocarbons. The pour point of a sample of straight-run kerosene (CAS No. 8008-20-6) with 15 - 20% aromatics was measured by API (1987b) to be –55 °C. The pour point values for three jet fuels reported by Jokuty et al. (2002) ranged from –50 to –47 °C. Therefore steam-cracked distillates is expected to have a pour point less than -47°C.

Boiling Point

Refinery process streams do not have a single numerical value for boiling point, but rather a boiling or distillation range that reflects the range of individual constituents in the substance (ASTM D2887). The measured distillation data on a sample of steam-cracked distillates ranged from 67 *°C to 220 °C (152 °F to 428 °F*).

Vapor Pressure

Raoult's Law states that the vapor pressure of solutions is the sum of the products of the vapor pressures of each individual constituent multiplied by its mole fraction in the complex substance. Steam-cracked distillates is expected to have a measurable vapor pressure due to the measured boiling range 67 *°C to 220 °C (152 °F to 428 °F*) and molecular weights of the constituent hydrocarbons (C5 – C18 carbon atoms). Measurements indicate that a range of 1290 hPa to 9150 hPa may be considered typical vapor pressures for members of the gasoline blending streams category (CONCAWE, 1996a). The vapor pressures of kerosene (API, 1987b) and Jet A/A-1 (Jokuty et al., 2002) measured at 37.8 °C using ASTM D323 were 14 hPa and >10 hPa, respectively. Therefore steam-cracked distillates is expected to have a range of vapor pressures of up to 9150 hPa.

Octanol:Water Partition Coefficient

The percent distribution of the hydrocarbon groups (i.e., paraffins, olefins, naphthenes, and aromatics) and the carbon chain lengths of hydrocarbon constituents in steam-cracked distillates determine the partitioning characteristics of the complex substance. Generally, hydrocarbon chains with fewer carbon atoms tend to have lower partition coefficients than those with higher carbon numbers (CONCAWE, 2001). The calculated partition coefficient values of the hydrocarbons in gasoline range hydrocarbons are expected to fall within the range 1.23 to 4.8 while kerosene range hydrocarbons have log Kow values of 3.3 to >6 determined by EPI-Suite™ (EPA, 2000). Therefore, steam-cracked distillates constituents are expected to have a range of log Kow values between 1.23 and >6.

Water Solubility

Water solubility values for the individual hydrocarbon constituents making up steam-cracked distillates vary by orders of magnitude. Both molecular weight and chemical structure influence the degree of solubility (Shiu, et al., 1990; Yaws, et al., 1994). The constituent hydrocarbons of gasoline blending streams (which are more soluble than kerosene/jet fuel constituents) have calculated solubility values ranging from <1 to 2000 mg/L (Petroleum HPV, 2008). The solubility of the constituents in steam-cracked distillates will be affected by the sample composition and the loading rates (water to oil ratio) used in the study. A predicted range of <1 to 2000 mg/L is recommended for steam-cracked distillates.

Environmental Fate

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

To assess the environmental fate properties for the HPV program, the U.S. EPA has selected important fate endpoints by which these substances may be characterized. Thus, environmental fate endpoints include the following:

photodegradation,

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

In determining these fate characteristics for steam-cracked distillates a high reliance was placed on predicted properties of the individual hydrocarbon constituents. These constituents were selected to span the expected ranges of molecular weights and hydrocarbon types in steam-cracked distillates. Therefore, the package of computer programs contained in EPI Suite™ (US EPA, 2000) was used to estimate the properties of photodegradation, stability in water, and environmental distribution. Measured data on gasoline blending streams and kerosene substances, when available, were also included in the assessment.

For the assessments of biodegradation, the approach taken was to characterize the biodegradability potential of the whole substance. Existing biodegradation data on gasoline blending streams and kerosene substances were reviewed.

Direct photodegradation

The direct aqueous photolysis of an organic molecule occurs when it absorbs sufficient light energy to result in a structural transformation. Only light energy at wavelengths between 290 and 750 nm can result in photochemical transformations in the environment, although absorption is not always sufficient for a chemical to undergo photochemical degradation (Harris, 1982a). Steam-cracked distillates does not contain component molecules that will undergo direct photolysis. Therefore, this fate process will not contribute to a measurable degradative removal of chemical components in this substance from the environment.

Indirect Photodegradation

Hydrocarbon constituents of steam-cracked distillates that readily volatilize to air may undergo a gas-phase oxidation reaction with photochemically produced hydroxyl radicals (OH^{-}). Atmospheric oxidation as a result of hydroxyl radical attack is not direct photochemical degradation, but rather indirect degradation (Schwarzenbach et al, 2003). Atkinson (1990) gives data which enables half-lives to be calculated for the degradation of hydrocarbons in contact with hydroxyl radicals under sunlight conditions in the troposphere. Half-life values for typical hydrocarbon constituents in gasoline and kerosene that volatilize to air are as follows:

Constituent	Half-life, days
Benzene	6.5
n-hexane	1.4
toluene	1.3
cyclohexane	1.1
n-decane	0.69
n-tetradecane	0.42
naphthalene	0.37
C16 2-ring aromatics	0.2

The half-life for volatile constituent of steam-cracked distillates is expected to be in the range of 0.2 to 6.5 days.

Stability in Water

Hydrolysis is unlikely for steam-cracked distillates. Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include alkylhalides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Harris, 1982b). The chemical components that comprise steam-cracked distillates are not subject to hydrolysis reactions with water.

Transport Between Environmental Compartments (Fugacity Modeling)

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

Results of Level I models are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical is likely to partition in the environment. One drawback of these and higher level models is their inability to predict the distribution of the entire set of constituents comprising complex petroleum streams. To gain an understanding of the potential environmental distribution for these complex substances, modeling was performed for individual hydrocarbon compounds that had been identified through detailed hydrocarbon analyses as existing in these streams. The hydrocarbons selected for modeling were not only those identified as existing in these substances, but they also spanned a wide range of molecular weights and hydrocarbon types. The resulting values represent the potential ranges of distribution to environmental media for those hydrocarbon constituents which could potentially be found in these streams:

Gasoline Blending Streams (C4 – 12) Petroleum HPV, 2008	**Kerosene/Jet Fuel Substances (C9 – C16)** Petroleum HPV, 2010
Air ≥ 96.5%	Air <1% to 99%
Water ≤2.7%	Water <0.1% to 8%
Soil ≤1.2%	Soil <1% to 97%
Sediment ≤0.03%	Sediment ≤2%
Suspended sediment≤0.02%	Suspended sediment <0.1%

Therefore based on modeling of individual chemical encompassing the different types and molecular weights of hydrocarbons making up steam-cracked distillates, volatilization to the atmosphere is predicted to be an important process.

Biodegradation

Petroleum hydrocarbon biodegradability is governed by the molecular structure of individual hydrocarbons and the metabolic capability of the exposed microbial community. In general, the smaller and simpler molecules (e.g., short-chain normal paraffins) are most readily degraded, while increased molecular weight, branching, presence of aromatic structures, and substitution tend to decrease the rate and sometimes the extent of biodegradation of hydrocarbons of the same carbon number (Atlas, 1981). The biodegradability of a complex substance such as steam-cracked distillates would be the sum of the partial biodegradability of each individual component.

Selected data for gasoline blending streams show that the components of these streams have the potential to biodegrade to a high extent. These data are based on test results for three streams; one composed primarily of isoparaffinic hydrocarbons (CAS #64741-66-8), a second consisted of isoparaffinic, olefinic, naphthenic and aromatic hydrocarbons (CAS #64741-55-5), and a third stream composed of linear paraffins, iso-paraffins and aromatic hydrocarbons (CAS #64741-63-5). These three streams were tested for inherent biodegradability by the modified ISO/DIS 14593 CO_2 evolution test (CO_2 headspace test) using acclimated inoculum (Springborn Laboratories, 1999a-c). The CO_2 headspace procedure employed a closed system, which is recommended when assessing the biodegradability of poorly water soluble and volatile substances like steam-cracked distillates.

Limited specific biodegradation data from studies utilizing standard test methodology are available for kerosene/jet fuels category members. Data are available on the behavior of one category member (straight-run kerosene, CAS no. 8008-20-6) following OECD 301F ready biodegradability test guidelines, indicating the refining stream is inherently, though not readily, biodegradable with an average 58.6% of theoretical oxygen consumption in 28 days (Mobil, 1999).

Results of the inherent biodegradability tests indicated a high capacity to biodegrade when the bacteria have been allowed to optimize their enzymatic activity during an acclimation period. While not expected to pass the criteria for ready biodegradability, the data show that steam-cracked distillates should not persist in the environment.

Ecotoxicity

Based on the studies identified to represent the acute toxicity of gasoline blending streams to aquatic organisms, the range of acute toxicities was generally similar for the three trophic levels (fish, invertebrates, and algae). The proposed “read-across” ranges of toxicity endpoints (expressed as lethal loading rates) that are expected to represent the potential acute toxicity to fish, invertebrates, and algae were 2.09 to 46 mg/L, 0.9 to 32 mg/L, and 1.1 to 64 mg/L, respectively (Petroleum HPV, 2008). The substances in the Kerosene/Jet Fuel Category were found to produce a narrower range of toxicity than gasoline blending streams for the aquatic species when studies using similar solution preparation and exposure techniques are compared. The proposed ranges of acute toxicity of kerosene substances (expressed as lethal loading rates)

that are expected to represent the potential toxicity are: Fish 18 – 25 mg/L, Invertebrates 1.4 – 21 mg/L, Algae 5.0 – 11 mg/L (Petroleum HPV, 2010). A commercial C9 Aromatic solvent was tested in fish and invertebrates for acute toxicity with water accommodated fractions and gave EC50 results of 9.2 mg/l (96-hr) and 6.1 mg/l (48-hr) respectively (Exxon, 1992a and Exxon, 1992b).

Because of the carbon number and boiling range of steam-cracked distillates, the aquatic toxicity is expected to be no greater than that observed for gasoline blending streams.

Human Health Effects

Acute Toxicity

Results of testing on gasoline blending streams (Petroleum HPV, 2008), kerosene/jet fuel category members (Petroleum HPV, 2010), and C9 Aromatics (IUCLID, 2000) for acute toxicity indicate that steam-cracked distillates is expected to demonstrate consistently low toxicity by the oral [Rat LD50 >5g/kg], dermal [Rabbit LD50 >2g/kg] and inhalation [Rat LC50 >5g/m^3] exposure routes. Steam-cracked distillates is expected to be a mild to moderate eye and skin irritant. No skin sensitization potential is anticipated.

Repeated Dose Toxicity

Results of repeat dose inhalation studies have demonstrated fairly similar profiles of toxicity across the 4 PONA chemical classes with gasoline blending streams (Petroleum HPV, 2008). Exposure to either the whole naphtha or distillate fractions (also referred to as “light-ends”) could result in alpha 2-uglobulin mediated nephropathy in kidneys of male rats, also identified as light hydrocarbon induced nephropathy, a species and sex specific syndrome not relevant to human health (US EPA, 1991). Other systemic toxicity was minimal and in general, included increased weight of the liver in most studies and of spleen with one aromatic sample, and some decreases in body weight or small changes in clinical pathology parameters. One distillate fraction of an olefinic stream induced a decrease in sperm number per gram of epididymis, an effect not supported by other measurements relative to male reproductive capacity in this study or other studies. In studies where neurotoxicity was evaluated none of the streams induced significant neurobehavioral or neuropathologic effects.

A petroleum distillate--a high aromatic naphtha--consisting of a 50/50 blended mixture of equivalent products. SHELLSOL A* and SOLVESSO 100**, containing C9 isomers (75 percent) particularly trimethyl benzenes, was examined for systemic toxicity in rats by inhalation exposure. A preliminary 13-week inhalation study with SHELLSOL A had resulted in liver and kidney weight increases in female rats at the high (7400 mg/m3) and medium (3700 mg/m3) exposure levels, and a low grade anaemia in females at all exposure levels (7400, 3700 and 1800 mg/m3) (Shell, 1980). The follow-up 12-month inhalation study in rats described here used atmosphere generated from the SHELLSOL A/SOLVESSO 100 blend of 1800, 900 and 450 mg/m3. Initial reduction in body weight gain occurred in both male and female rats at the higher exposures. Various statistically significant haematological changes were transiently seen in males up to six months, but were not considered biologically significant. High exposure male liver and kidney weights were increased at 6 and 12 months but, in the absence of histopathological changes, were considered to be physiological adaptive responses. No treatment-related histopathological abnormalities were found. It is concluded that chronic exposure to this high aromatic naphtha is without systemic toxicity in rats under the conditions of these studies (Shell, 1981 and Clark et al, 1989).

C9 Aromatics were evaluated for neurotoxicity after a 13-week repeat dose inhalation exposure (6hr/d, 5d/w) at concentrations of 101, 452, and 1320 ppm. In this study, other than a transient weight reduction in the high exposure group (not statistically significant at termination of exposures) No effects were noted on startle response, forelimb and hind limb grip strength, hind limb splay, or thermal response. No effects were noted on motor activity at any treatment level. Examination of sections of brain, cervical and lumbar spinal cord, and left and right proximal sciatic nerves failed to reveal any neurotoxic change (Douglas, et al, 1993).

The read-across value for inhalation of steam-cracked distillates is NOAEC = 1320 ppm.

A 13-week subchronic toxicity/neurotoxicity study was conducted with a sample of hydrodesulfurized kerosene (HDS) (Battelle, 1997). The sample met the specifications for aviation turbine fuel (Jet A). HDS kerosene was diluted in USP grade mineral oil (to avoid excessive dermal irritation) and applied to the shaved backs of Sprague-Dawley CD rats, 12/sex/group, 6 hr/d, 5 d/wk. Doses of 0 (vehicle control), 165 mg/kg (20% HDS kerosene), 330 mg/kg (40% HDS kerosene), or 495 mg/kg (60% HDS kerosene) were used. The high dose was selected based on previous studies in which it was shown that dilution of HDS kerosene to concentrations below 60% in moderate viscosity (340 SUS) USP mineral oil prevented the development of excessive dermal irritation. Additional rats (12/sex) in the control and high dose groups were held after final treatment for a 4-week recovery period. HDS kerosene produced a dose-related increase in skin irritation at the site of administration with an apparent greater effect in males. Histopathology confirmed minimal, reversible, skin lesions. Hematology results were unremarkable except for an elevation in the mean neutrophil values for the high dose females and possibly males. All hematology values were normal after 4-weeks recovery. There were no apparent test-related effects on neurotoxicological endpoints and no gross or microscopic findings in peripheral or central nervous system tissues. Statistically significant increases in relative spleen weight at treatment termination and in absolute spleen weight after the recovery period were observed in high dose females without gross or microscopic correlate. The NOAEL for neurotoxicity was 495 mg/kg/day and for subchronic toxicity (excluding skin irritation) the NOAEL was 330 mg/kg/day.

Therefore the read-across NOAEL value for steam-cracked distillates s is 330 mg/kg for dermal exposure.

Genetic Toxicity In Vitro

Results from representative samples from each of the PONA categories indicate that most gasoline blending streams are not mutagenic in mammalian cells but there were some with high aromatic content in which equivocal or in one case positive activity was seen with metabolic activation (Petroleum HPV, 2008). Gasoline tested in both bacterial and mammalian cell assays did not induce mutation in either test system. Kerosenes and jet fuels have been tested in a number of mammalian and bacterial assay systems with predominately negative results (Petroleum HPV, 2010). For C9 Aromatics, in vitro genotoxicity studies included the *Salmonella*/mammalian microsome mutagenicity assay, the hypoxanthine-guanine phosphoribosyl transferase (HGPRT) forward mutation assay in CHO cells, and *in vitro* chromosome aberration and sister chromatid exchange (SCE) assays in CHO cells. There was no evidence that C9 Aromatics was either a gene or chromosomal mutagen (Schreiner, et al, 1989).

Steam-cracked distillates is not predicted to be an *in vitro* mutagen either with or without metabolic activation.

Genetic Toxicity In Vivo

All PONA categories are negative for induction of chromosome aberrations in rats. One high olefinic sample induced sister chromatid exchanges (SEC) in mice. The same test material gave negative results in two cytogenetic assays in rats (Petroleum HPV, 2008). Gasoline did not induce cytogenetic damage in rats or have any adverse effects on spermatogenic cycle in mice. Although SCEs were induced in rats exposed to gasoline light-ends at concentrations over 2000 mg/m^3 for 28-days, the parallel micronucleus study was negative (API, 2005b and 2005c).

An *in vivo* chromosome aberration assay in rat bone marrow with C9 Aromatics was negative (Schreiner, et al, 1989).

Deodorized kerosene and Jet A produced negative results in dominant lethal assays (API, 1973, 1980b). The deodorized kerosene was administered by ip and subcutaneously routes to rats and mice respectively at 1 g/kg. The Jet A was administered to mice by inhalation of 100 or 400 ppm for six hours a day for eight weeks. McKee et al. (1994) tested five middle distillate materials, including Jet Fuel A, by gavage, in the CD-1 mouse bone marrow micronucleus test. No increases in the frequency of MNs were observed for any of the test materials in assessments 24, 48, or 72 hr after treatment. The authors did not see any evidence of bone marrow depression. Vijayalaxmi et al., (2006) investigated the genotoxic potential of jet fuels, JP-8 and Jet-A. Mice were treated dermally with either single or multiple applications of these jet fuels. Peripheral blood and bone marrow smears were prepared to examine the incidence of micronuclei (MN) in polychromatic erythrocytes (PCEs). In all experiments, using several different exposure regimens, no statistically significant increase in the incidence of MN was observed in

the bone marrow and/or peripheral blood of mice treated with JP-8 or Jet-A when compared with those of untreated control animals.

The results of micronucleus tests on a range of petroleum HPV category substances also support the conclusion that clastogenic effects are unlikely to be induced by steam-cracked distillates (McKee *et al*, 2010).

Steam-cracked distillates is not predicted to be an *in vivo* mutagen either with or without metabolic activation.

Reproductive and Developmental Toxicity

Consistent evidence of developmental or reproductive toxicity was not observed in inhalation studies in rats for whole naphtha or distillate fractions (also referred to as "light-ends").In addition, no developmental effects were seen with wholly vaporized gasoline [NOAEC = 1600ppm (5970mg/m^3)], a 10% distillate fraction of unleaded gasoline [NOAEC= 8993ppm (23881mg/m^3)], or gasoline light-ends [NOAEC = 20,638 mg/m^3] or in two 2-generation reproduction studies with vapor recovery gasoline or gasoline light-ends [NOAEC ≥ 20,000mg/m^3in both studies]. No increases in resorptions were reported in any of these studies. As there were no consistent differences between paraffinic, olefinic, naphthenic and aromatic streams, NOAEL values for developmental and reproductive effects in studies of gasoline and naphtha streams were the maximum doses tested (Petroleum HPV, 2008).

C9 Aromatics were tested for developmental toxicity in CD-1 mice by inhalation exposure to concentrations of 100, 500, or 1500 ppm. Developmental toxicity was observed at the 500 and 1500 ppm dose levels. This was manifested as a significant increase in mean post-implantation loss at 1500 ppm, and significant decreases in mean fetal body weights at 500 and 1500 ppm levels. Evidence of delayed fetal development also included increased incidence of unosssified sternebrae and reduced skull ossification at 1500 ppm as compared to controls. Maternal toxicity included near 50% mortality, reduced food intake and inhibited body weight gain during exposure and overall gestation period and significant decreases in mean hematocrit and mean corpuscular hemoglobin concentration at 1500 ppm. There were also maternal effects at 500 ppm. The NOAEC for maternal and developmental toxicity was 100 ppm. (McKee et al, 1990).

C9 Aromatics were testing for reproductive toxicity in SD rats by inhalation exposure to concentrations of 103, 495 1495 ppm in a 3 (three) generation reproductive study. Animals in the F0,F1, and F2 generations were exposed for 10 weeks prior to mating. Mortality in the F1, F2, and F3 generations was observed in the 1480 ppm treated groups. The LOAEC with respect to F0 and F1 parental systemic toxicity was 495 ppm, based on reduced body weights observed in the F2 generation. The developmental LOAEC was determined to be 495 ppm based on reduced body weight in the F3 pups; maternal body weight was also reduced in the 495 ppm treated group. No reproductive effects were observed at the highest dose tested. However, a full evaluation of the 1480 ppm F2 generation was precluded due to excessive mortality (only six dams available); no reproductive effects were observed in these dams

Systemic Effects on Parental Generations: The F0 males showed statistically and biologically significantly decreased mean body weight by ~15% at 1480 ppm when compared with controls. Seven females died or were sacrificed in extremis at 1480 ppm. The F1 parents at 1480 ppm had statistically significantly decreased mean body weights (by ~13% (females) and 22% (males)), and motor activity. The female rats in the 495 ppm exposed group had a 13% decrease in body weight gain when adjusted for initial body weight when compared to control. F1 parents at this concentration also had increased ataxia and mortality (six females). Most F2 parents (70/80) exposed to1480 ppm died within the first week of exposure. The remaining animals survived throughout the rest of the exposure period. At week 4 and continuing through the study, F2 parents at 1480 ppm had statistically significant mean body weights much lower than controls (~33% for males; ~28% for females); body weights at 495 ppm were also reduced significantly (by 13% in males and 15% in females). The male rats in the 495 ppm exposed group had a 12% decrease in body weight gain when adjusted for initial body weight when compared to control. Based on reduced body weight observed in the F2 generation, the overall systemic toxicity LOAEC is 495 ppm (2430 mg/m3).

Reproductive Toxicity - Effects on Parental Generations: There were no pathological changes noted in the reproductive organs of any animal of the F0, F1, or F2 generation. No effects were reported on sperm morphology, gestational period, number of implantation sites, or

post-implantation loss in any generation. Also, there were no statistically or biologically significant differences in any of the reproductive parameters, including: number of mated females, copulatory index, copulatory interval, number of females delivering a litter, number of females delivering a live litter, or male fertility in the F0 or in the F2 generation. Male fertility was statistically significantly reduced at 1480 ppm in the F1 rats. However, male fertility was not affected in the F0 or in the F2 generations; therefore, the biological significance of this change is unknown and may or may not be attributed to the test substance. No reproductive effects were observed in the F0 or F1 dams exposed to 1480 ppm (7265 mg/m3). Due to excessive mortality at the highest concentration (1480 ppm, only six dams available) in the F2 generation, a complete evaluation is precluded. However, no clear signs of reproductive toxicity were observed in the F2 generation. that can be attributed to the test substance were observed in any generation or at any concentration. Therefore, the reproductive NOAEC is considered 495 ppm (2430 mg/m3), which excludes analysis of the highest concentration due to excessive mortality.

Developmental Toxicity - Effects on Pups: Because of significant maternal toxicity (including mortality) in dams in all generations at the highest concentration (1480 ppm), effects in offspring at 1480 ppm are not reported here. No significant effects were observed in the F1 and F2 generation offspring at 103 or 495 ppm. However, body weights and body weight gain were reduced by (~ 10-11%,) in the F3 offspring were lower than at 495 ppm for approximately a week (PND 14 through 21) when compared to controls. Maternal body weight was also depressed (by ~ 12%) throughout the gestational period when compared with controls. The overall developmental LOAEC from this study is 495 ppm (2430 mg/m3) based on the body weights reductions observed in the F3 offspring (McKee et al, 1990).

The read-across ranges for inhalation of steam-cracked distillates are:

Systemic LOAEC = 495 ppm
Developmental LOAEC = 495 ppm
Reproductive NOAEC = 495 ppm, which excludes analysis of the highest concentration due to excessive mortality.

A reproductive/developmental screening study in Sprague-Dawley rats of hydrodesulfurized kerosene (Schreiner et al., 1997) was performed in accordance with OECD Guideline 421, except males were treated for 8 weeks to improve the quality of the assessment of the reproductive toxicity assessment. Doses of 0, 20, 40 or 60% (v/v) kerosene in mineral oil were applied to the skin of the rats. The doses per body weight equivalents were 0, 165, 330 and 495 mg/kg. Test material was applied daily, 7 days/week from 14 days premating through 20 days of gestation. There were no treatment-related effects on mortality and no clinical signs of toxicity were observed. Compound-related skin irritation (usually graded as slight) was seen in both males and females. At the terminal sacrifice, no findings were reported except for those on the skin. Over the course of the 8 weeks, high dose males gained less weight than the controls; however, body weights and food consumption were unaffected by treatment. High dose males had a higher mean relative kidney weight than controls, this being attributed to the lower mean final body weights of the high dose group. Microscopic changes were found in the skin of males in the vehicle control and all kerosene-treated groups. In females, the skin changes were observed only in the high dose group, but there were no other effects. No test-material-related microscopic changes were observed in the testes or epididymides of adult male rats or in the ovaries of adult female rats. There were no compound-related effects on any of the reproductive/developmental parameters. The authors concluded that the no observable effect level (NOEL) for reproductive/developmental toxicity of HDS kerosene under the treatment conditions of the study was 495 mg/kg/day. Steam-cracked distillates would be predicted to have a NOEL of approximately 495 mg/kg.

Therefore the read-across NOAEL values for reproductive and developmental endpoints for steam-cracked distillates are 100 ppm for inhalation exposure and 495 mg/kg for dermal exposure.

Exposure

Steam-cracked distillates is expected to only be used commercially rather than sold as a separate product. There is no expected exposure to consumers or children.

Potential occupational exposures to steam-cracked distillates would be controlled by appropriate protective clothing for dermal contact and air monitoring for potential inhalation exposures. There are enforceable (OSHA Permissible Exposure Limits) and recommended (ACGIH Threshold Limit Values) occupational exposure standards for numerous volatile constituents expected to be in steam-cracked distillates. Examples of these standards are shown in Table 3.

Table 3. OSHA and ACGIH Occupational Exposure Standards for Some Volatile Constituents of Steam-cracked distillates (8-hour Time Weighted Averages)

Carbon Number		C5	C6	C7	C8	C9	Others
Component OSHA and/or ACGIH Occupational Exposure Standard		**Pentane** **OSHA** 500 ppm (n-pentane) **ACGIH** 600 ppm (all isomers)	**Benzene** **OSHA** 1 ppm **ACGIH** 1 ppm	**Toluene** **OSHA** 200 ppm **ACGIH** 20 ppm	**Xylenes** **OSHA** 100 ppm **ACGIH** 100 ppm	**Cumene** **OSHA** 50 ppm **ACGIH** 50 ppm	**Gasoline** **ACGIH** 300 ppm
			Hexane **OSHA** 500 ppm **ACGIH** 50 ppm			**Trimethyl Benzene** **ACGIH** 25 ppm (all isomers)	**Kerosene** **ACGIH** **200 mg/m^3 vapor**

Data Matrix

Endpoint	Supporting Chemical 64742-95-6	Data from the Gasoline Blending Streams Category	Data from the Kerosene/Jet Fuel Category	Read-Across to Steam-cracked distillates
Pour Point (°C)	-	-55	-50 to -47	< -47
Boiling Range (°C)	-			6 – 314
Vapor Pressure (hPa)	-	1290 to 9150	>10	>10 to 9150
Partition Coefficient	-	1.23 to 4.8	3.3 to >6	1.23 to >6
Water Solubility (mg/L)	-	<1 to 2000		<1 to 2000
Photodegradation, OH^- reaction $T_{1/2}$ (h or d)	-	0.37 to 6.5 d	0.2 to 1.5 d	0.2 to 6.5 d
Stability in Water	-	Stable	Stable	Stable
Environmental Distribution	-	Air ≥96.5% Water <=2.7% Soil <=1.2%	Air <1% - 99% Water <0.1% - 8% Soil <1% - 97%	Mainly to air
Biodegradation	-	Inherently biodegradable	Inherently biodegradable	Not readily Biodegradable
Acute Fish LL50 (mg/L WAF loading rate)	9.2	2.09 to 46	18 to 25	2.09 to 46
Acute Daphnia EL50 (mg/L WAF loading rate)	6.1	0.9 to 32	1.4 to 21	0.9 to 32
Algae EL50 (mg/L WAF loading rate)	-	1.1 to 64	5 to 11.0	1.1 to 64
LD_{50} Dermal	>2 g/kg		>2 g/kg	>2 g/kg
LC_{50}	>5 g/m^3	>5 g/m^3		>5 g/m^3
Repeat Dose (inhalation)	NOAEC = 1320 ppm	NOAEC = 10,153mg/m^3 (light-ends)		1320 ppm
Repeat Dose (dermal)			330 mg/kg/d	330 mg/kg/d
In vitro Mutagenicity	Negative	Negative	Negative	Negative
In vivo Mutagencity	Negative	Negative	Negative	Negative
Developmental Toxicity (inhalation)	NOAEC = 100 ppm	NOAEC > 20,638mg/m^3 (light-ends)		NOAEC = 100 ppm
Developmental Toxicity (dermal)			495 mg/kg/d	495 mg/kg/d
Reproductive Toxicity (inhalation)	NOAEC = 495ppm	NOAEC > 20,004 mg/m^3 (light-ends)		NOAEC = 495 ppm
Reproductive Toxicity (dermal)			>495 mg/kg/d	>495 mg/kg/d

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List of Abbreviations and Acronyms

API – American Petroleum Institute

BOD – biological oxygen demand

Btu/lb – British thermal unit per pound

Btu/scf – British thermal unit per standard cubic feet

AUGC – area under the growth curve

CAS RN/CAS #/CAS No. - Chemical Abstract Service Registry Number

^{o}C – degrees Celsius

CONCAWE – Conservation of Clean Air and Water in Europe

d - day

DMSO – Dimethyl sulfoxide

EINECS – European Inventory of Existing Commercial Chemical Substances

EL_{50} – effective loading rate lethal to 50% of the test population

E_bL_{50} – effective loading rate that causes 50% reduction in algal cell biomass

E_rL_{50} – effective loading rate that causes 50% reduction in algal growth rate

EPA/US EPA – United States Environmental Protection Agency

g/cm^3 – grams per cubic centimeter

h - hour

HLS – Huntingdon Life Sciences

HPV – High Production Volume

IRDC – International Research and Development Corporation

^{o}K – degrees Kelvin

kPa - kilopascal

LC_{50} – lethal concentration for 50% of the test population

LD_{50}– lethal dose level for 50% of the test population

LL_{50} – lethal loading rate for 50% of the test population

Loading Rate – total amount of test substance added to dilution water to prepare water accommodated fractions (WAFs) for ecotoxicity testing

LOAEL – lowest observable adverse effect level

mg/kg – milligrams per kilogram

mg/L – milligrams per liter

mg/m^3 – milligrams per cubic meter

mL - milliliter

mm - millimeter

nm - nanometer

NOAEL – no observable adverse effect level

NOEC – no observable effect concentration

NOELR – no observable effect loading rate

OECD – Organization for Economic Cooperation and Development

OPPTS – US EPA Office of Prevention, Pesticides and Toxic Substances

PAC - Polycyclic aromatic compound

PAH – polycyclic aromatic hydrocarbon

PNA – polynuclear aromatic

ppm – part per million

SIDS – Screening Information Data Set

US EPA – United States Environmental Protection Agency

UV - ultraviolet

WAF – water accommodated fraction

wt% - weight percent

μg - microgram

μg/L – microgram/liter

> greater than

< less than

= equal to

Glossary

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

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

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

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

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

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

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

Fish, Acute Toxicity Test: In a four-day exposure, acute toxicity is defined by the LC_{50}, the concentration of test substance in water which kills 50% of the test population of fish. Test methodology is described in OECD Guideline 203, in OECD Guidelines for the Testing of Chemicals.

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

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

Endpoint: In the context of the EPA High Production Volume Challenge Program, an endpoint is a physical-chemical, environmental fate, ecotoxicity, and human health attribute measurable by following an approved test methodology (e.g., OECD Guidelines for Testing of Chemicals).

Melting point, biodegradation, fish acute toxicity, and genetic toxicity are examples of endpoints that are measured by an approved test method.

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

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

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

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

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

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

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

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

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

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

Hazard: A potential source of harm.

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

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

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

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

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

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

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

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

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

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

Portal of Entry Effect: A local effect produced at the tissue or organ of first contact between the biological system and the toxicant.

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

Systemic Effects or Systemic Toxicity: Toxic effects as a result of absorption and distribution of a toxicant to a site distant from its entry point.

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

Appendix 1. IUCLID, 2000 OECD dossier for Solvent naphtha (petroleum), light aromatic (CAS 64742-95-6)