U.S. EPA HPV Challenge Program

HPV Chemical Hazard Characterization for

Naphtha (petroleum), heavy coker
CAS Number 68333-23-3

Submitted by:
Petroleum HPV Testing Group
Consortium Registration #1100997

American Petroleum Institute
1220 L Street NW
Washington, DC 20005
www.petroleumhpv.org

Submission date
January 25, 2011

Table of Contents

List of Tables, Figures, and Appendices

Summary

Naphtha (petroleum), heavy coker (hereafter called thermocracked naphtha) has the Chemical Abstract Services (CAS) number 68333-23-3 and the following CAS definition, *A complex combination of hydrocarbons from the distillation of products from a fluid coker. It consists predominantly of unsaturated hydrocarbons having carbon numbers predominantly in the range of C6 through C15 and boiling in the range of approximately 157°C to 288°C (315°F to 550°F).*

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, environmental effects and human health effects for thermocracked naphtha can be predicted from data in those previously submitted categories.

The measured distillation data on samples of thermocracked naphtha ranged from 6°*C to 314°C (42°F to 598°F).* Based on the carbon range of up to C15, freezing points of less than -40°*C* would be expected. The physical-chemical characteristics of the thermocracked naphtha also include an estimated range of vapor pressures between 10 hPa to 9150 hPa, indicating some tendency to volatilize. For constituent hydrocarbons in thermocracked naphtha, 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 thermocracked naphtha 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 thermocracked naphtha, 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 thermocracked naphtha (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 for the same aquatic species when studies using similar solution preparation and exposure techniques were compared.

Because of the carbon number range found in thermocracked naphtha, both inhalation and dermal routes of exposure are considered relevant in assessing the potential for human health hazards. Data on gasoline blending streams 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 and kerosene/jet fuel category members for acute toxicity lead to predictions that thermocracked naphtha 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. Thermocracked naphtha is expected to be a mild to moderate eye and skin irritant. No skin sensitization potential is anticipated.

As there were no appreciable differences in repeat dose toxicity between the inhalation toxicity values for paraffinic, olefinic, naphthenic and aromatic naphtha streams, the lowest value derived from all repeat dose toxicity studies has been used to read-across to thermocracked naphtha. A 90-day repeat dose study on hydrodesulfurized kerosene was used to predict the dermal NOAEL. The read-across values for thermocracked naphtha are: 10,153mg/m^3 (light-ends) for inhalation and 330 mg/kg/d for dermal exposure. There were no significant effects on the reproductive organs of male and female rats from either gasoline blending streams or kerosene/jet fuel substances in repeat dose studies.

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. The read-across conclusion for thermocracked naphtha 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. The read-across conclusion for thermocracked naphtha is that it will not be genotoxic under *in vivo* conditions.

As there were no appreciable differences between the inhalation toxicity of paraffinic, olefinic, naphthenic and aromatic naphtha streams, the lowest NOAEC derived from all developmental toxicity studies has been used to read-across to thermocracked naphtha. The NOAEL from an OECD 421 reproductive-developmental screening study on hydrodesulfurized kerosene study was used to evaluate the dermal hazard. The read-across values for developmental toxicity are: For inhalation an NOAEC > 20,638mg/m^3 (light-ends)and for dermal exposure a NOAEL of 495 mg/kg/d.

Read-across data from repeat dose and developmental studies on gasoline blending streams and kerosene/jet fuel substances are sufficient to assess the reproductive toxicity of thermocracked naphtha. In addition, two multi-generation reproduction studies have been done on gasoline vapor (light-ends) with NOAECs of over 20,000 mg/m^3. Based on those data, thermocracked naphtha is not expected to be a significant reproductive toxicant.

1. Introduction

Naphtha (petroleum), heavy coker (hereafter called thermocracked naphtha) has the Chemical Abstract Services (CAS) number 68333-23-3 and the following CAS definition; *A complex combination of hydrocarbons from the distillation of products from a fluid coker. It consists predominantly of unsaturated hydrocarbons having carbon numbers predominantly in the range of C6 through C15 and boiling in the range of approximately 157°C to 288°C (315°F to 550°F).* Seven facilities in the USA reported manufacturing thermocracked naphtha in 2006 (EPA, 2006).

Thermocracked naphtha is a substance generated by a petroleum refinery process with the generic name of thermal cracking (OSHA, 1999). Because the simple distillation of crude oil produces some streams that do not meet the technical requirements for finished fuels or lubricants, further refining may be used to alter the molecular structure of the hydrocarbons to add value. One of the ways of accomplishing this change is through "cracking," a process that breaks or cracks certain heavier, higher boiling-point petroleum fractions into more valuable products such as gasoline, fuel oil, and gas oils. The two basic types of cracking are thermal cracking, using heat and pressure, and catalytic cracking. The first thermal cracking process was developed around 1913. Distillate fuels and heavy oils were heated under pressure in large drums until they cracked into smaller molecules with better antiknock characteristics. This early process has evolved into the following applications of thermal cracking: visbreaking, steam cracking, and coking.

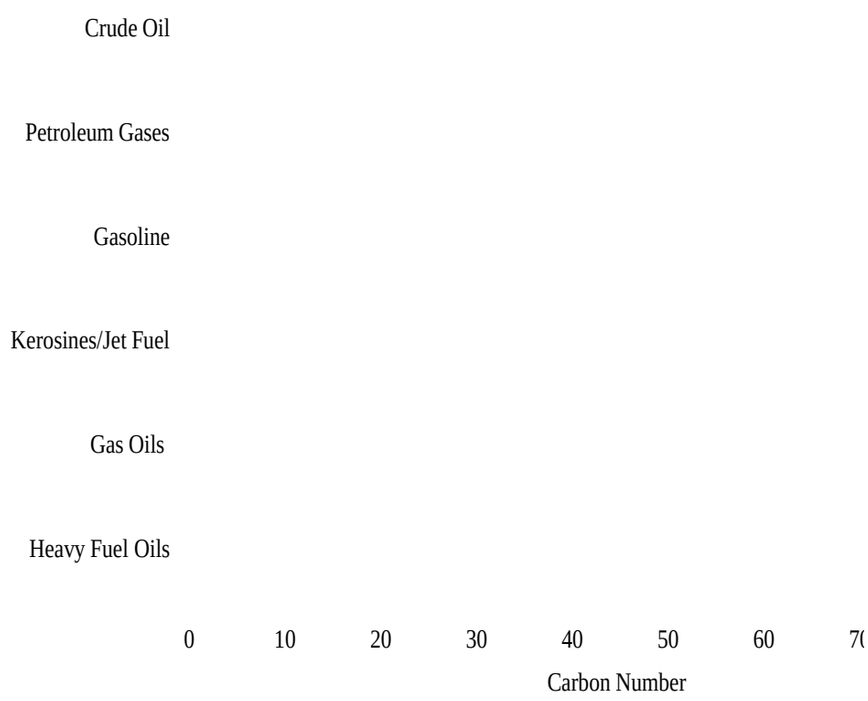
Thermocracked naphtha is a substance generated by a specific petroleum refinery process called “continuous coking” (OSHA, 1999). Coking is a severe method of thermal cracking used to upgrade heavy residual streams into lighter products or distillates. Coking produces straight-run gasoline (coker naphtha) and various middle-distillate fractions used as catalytic cracking feedstock. The process so completely removes hydrogen that the residue is a form of elemental carbon called "coke." The two most common processes are delayed coking and continuous (contact or fluid) coking. Continuous (contact or fluid) coking is a moving-bed process that operates at temperatures higher than delayed coking. In continuous coking, thermal cracking occurs by using heat transferred from hot, recycled coke particles to feedstock in a radial mixer, called a reactor, at a pressure of 50 psi. Gases and vapors are taken from the reactor, quenched to stop any further reaction, and fractionated. The reacted coke enters a surge drum and is lifted to a feeder and classifier where the larger coke particles are removed as product. The remaining coke is dropped into the preheater for recycling with feedstock. Coking occurs both in the reactor and in the surge drum. The process is automatic in that there is a continuous flow of coke and feedstock.

Refineries that produce thermocracked naphtha may blend it into various fuels (i.e., gasoline, jet fuel) depending on the specific properties of the material produced and the volume produced. Wherever it is used, the specifications for the finished commercial products must be met.

2. Composition of Naphtha (petroleum), Heavy Coker

The CAS definition for thermocracked naphtha contains an internal inconsistency between the carbon range and the boiling range. The expected boiling range for C6 through C15 hydrocarbons would be 36°C to 271°C (97°F to 520°F) (ASTM 2887). That boiling range would suggest significant amounts of gasoline blending stock would be present. However, the CAS definition cites a boiling range of 157°C to 288°C *(315°F to 550°F).* That boiling range would suggest significant amounts of kerosene blending stock would be present. It is the expectation of this category assessment document that thermocracked naphtha can contain constituents that span the range of both gasoline and kerosene (as illustrated in Figure 1).

Figure 1. Carbon Number Ranges for Various Petroleum HPV Categorie



Gasoline blending streams and kerosene/jet fuel category members are complex petroleum substances consisting of saturated hydrocarbons (normal and branched-chain **P**araffins), unsaturated hydrocarbons (**O**lefinic), **N**aphthenic hydrocarbons (cycloparaffins), and **A**romatic hydrocarbons. These four basic chemical classes are generally present to some degree in all gasoline blending streams and kerosenes. Paraffins, Olefins, Naphthenes and Aromatics are identified by the acronym PONA. As with most liquids from thermal cracking processes, the CAS definition suggests that thermocracked naphtha contains a substantial amount of unsaturated hydrocarbons (olefins).

Manufacturers that are members of the Petroleum HPV Testing Group were asked to provide analytical information on their thermocracked naphthas. Table 1 summarizes the available data.

Table 1. Boiling Range and PONA Distribution of Thermocracked Naphtha Samples

Boiling Range ^{0}F	**A-1**	**A-2**	**A-3**	**B-1**	**B-2**	**C-1**
T5%	91	89	99	297	42	277
T50%	242	245	259	436	236	327
T95%	343	347	359	598	356	474
PONA						
Paraffins	43.5	42.7	42.9	48.6 [P, N]	NDA	77.4 [P, N]
Olefins	23.8	23.8	21.3	24	NDA	15.1
Naphthenics	15.7	15.6	13.7	See above	NDA	See above
Aromatics	9.4	9.9	11.8	27.4	NDA	7.6

The boiling ranges of the six samples suggest that some refineries operated the continuous coking process to increase gasoline production while others may have been optimized for increased jet fuel production. (Operations can also be dependent on the season and local demand for products.) The olefin content of the samples (15 – 24 %) reflects the thermal cracking process they have been through. Crude oil has no measureable olefin content. Only cracking processes like catalytic cracking or coking create unsaturated hydrocarbons.

To evaluate the distribution of polycyclic aromatic compounds in thermocracked naphtha, a sample was analyzed by published methods (Roy et al., 1985 & 1988). The data presented in Table 2 show that only one and two ring compounds were present, results similar to those obtained with several kerosene/jet fuel substances (Petroleum HPV, 2010).

Table 2. Analysis of Thermocracked Naphtha for Polycyclic Aromatic Compounds

	DMSO wt.%	% ARC 1	% ARC 2	% ARC 3	% ARC 4	% ARC 5	% ARC 6	% ARC 7
Sample C-1	0.4	0.1	0.3	0.0	0.0	0.0	0.0	0.0

3. Rationale for Predicting the Range of SIDS Endpoints

The CAS definition of thermocracked naphtha 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}). Measured data on thermocracked naphtha for distillation range, PONA distribution and PAC profile support that conclusion. Therefore the range of physical & chemical properties, environmental fate, environmental effects and human health effects for thermocracked naphtha can be predicted from data in those previously submitted categories. The values predicted for thermocracked naphtha are bounded by the Gasoline Blending Streams Category or the Kerosene/Jet Fuel Category. Both inhalation and dermal routes of exposure are considered relevant.

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.

4. 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 the substances in the category, 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 thermocracked naphtha.

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 molecular weight range (C_4 to C_{16} 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 thermocracked naphtha 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). Distillation ranges (T5 to T95) for several samples of thermocracked naphtha are presented in Table 1. The measured distillation data on samples of thermocracked naphtha ranged from 6°*C to 314°C (42°F to 598°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 multipled by its mole fraction in the mixture. Thermocracked naphtha is expected to have a measurable vapor pressure due to the measured boiling range (6°C to 314°C (42°F to 598°F)) and molecular weights of the constituent hydrocarbons (C6 – C15 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 thermocracked naphtha is expected to have a range of vapor pressure of >10 hPa 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 thermocracked naphtha 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, thermocracked naphtha 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 thermocracked naphtha 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 thermocracked naphtha 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 thermocracked naphtha.

5. Environmental Fate

When a complex substance such as thermocracked naphtha 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 thermocracked naphtha 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 thermocracked naphtha. 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). Thermocracked naphtha 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 thermocracked naphtha 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-butane	3.2
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 thermocracked naphtha is expected to be in the range of 0.2 to 6.5 days.

Stability in Water

Hydrolysis is unlikely for thermocracked naphtha. 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 thermocracked naphtha 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 thermocracked naphtha, 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 substance such as thermocracked naphtha 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 thermocracked naphtha.

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 thermocracked naphtha should not persist in the environment.

6. 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).

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

7. Health Effects

A. Acute Toxicity

Results of testing on gasoline blending streams (Petroleum HPV, 2008) and kerosene/jet fuel category members (Petroleum HPV, 2010) for acute toxicity indicate that thermocracked naphtha 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. Thermocracked naphtha is expected to be a mild to moderate eye and skin irritant. No skin sensitization potential is anticipated.

B. 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. The read-across value for thermocracked naphtha is NOAEC = 10,153mg/m^3 (light-ends) (2880ppm total hydrocarbon determined as parts-per-million (ppm) hexane equivalents.)

Dermal irritation from repeated exposure to kerosene range substances is recognized as a significant experimental toxicology issue (Nessel,1999). Repeated administration will cause severe skin injury in many common animal models. The use of a mineral oil reduces skin irritation, allowing these substances to be repeatedly applied without producing skin injury when that is required by the study design.

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 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 determined in previous studies demonstrating an acceptable level of dermal irritation when HDS kerosene was diluted below 60% with moderate viscosity (340 SUS) USP mineral oil. 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 values for thermocracked naphtha are 10,153mg/m^3 (light-ends) for inhalation exposure and 330 mg/kg for dermal exposure.

C. 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 except for those substances with high aromatic content where 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).

Thermocracked naphtha 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 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).

Deodorized kerosene and Jet A produced negative results in dominant lethal assays (API, 1973, 1980b). The deodorized kerosene was administered either ip or subcutaneously in 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) evaluated five middle distillate materials, including Jet Fuel A, administered 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 a 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 support the conclusion that clastogenic effects are unlikely to be induced by thermocracked naphtha (McKee *et al*, 2010).

D. Reproductive and Developmental Toxicity

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 any PONA class with the exception of one olefinic naphtha sample [chamber vapor content 41% olefins] developmental study in which increased resorptions were reported at the highest dose [2128ppm; (7660mg/m^3)]. Of note is that the authors were not sure of the biological significance of this occurrence. A distillate fraction of the same CAS number with higher olefin content [chamber vapor content 61% olefins] run at higher exposure concentrations did not show any developmental toxicity. 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] nor 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. Based on the absence of increased resorptions with naphthas and gasoline in other study results and the opinions of the authors themselves, it was concluded that the increase in resorptions seen in the olefinic vapor sample may have been unique to that test sample and is not considered representative of naphtha streams in general. This study has not been used to establish the lower limit of the read-across range. As there were no other appreciable differences between paraffinic, olefinic, naphthenic and aromatic streams, a range of values derived from all developmental and reproductive toxicity studies have been used to read-across to naphtha hydrocarbon wastes (Petroleum HPV, 2008). NOAEL values for developmental and reproductive effects reflect the maximum doses tested. The read-across ranges for inhalation of thermocracked naphtha are:

Developmental NOAEC > 20,638mg/m^3 (light-ends)
Reproductive NOAEC > 20,004 mg/m^3 (light-ends)

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 potential for kerosene to affect on the male reproductive system. Doses of 0, 20, 40 or 60% (v/v) kerosene in mineral oil was 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. Thermocracked naphtha would be predicted to have a NOEL of approximately 495 mg/kg.

Therefore the read-across NOAEL values for reproductive and developmental endpoints for thermocracked naphtha are >20,000 mg/m^3 (light-ends) for inhalation exposure and 495 mg/kg for dermal exposure.

8. Exposure

Thermocracked naphtha is expected to be used as a refinery blending stock to produce fuels (i.e., gasoline, jet fuel) rather than sold as a separate product. There is no expected exposure to consumers or children. Thermocracked naphtha is likely to be blended with other refinery streams and then receive additional processing, such as hydrotreating, to achieve the necessary specifications for commercial gasoline or jet fuel. Gasoline and kerosene are widely distributed in commerce. Recent exposure assessment reports on both products are available from CONCAWE at http://www.concawe.be (Report No. 5/09 Additional human exposure information for gasoline substance risk assessment (period 2002-2007) and Report No. 6/07 Human exposure information for EU substance risk assessment of kerosene).

Potential occupational exposures to thermocracked naphtha 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 thermocracked naphtha. Examples of these standards are shown in Table 3.

Table 3. OSHA and ACGIH Occupational Exposure Standards for Some Volatile Constituents of Gasoline Blending Streams (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	**Ethyl Benzene** **OSHA** 100 ppm **ACGIH** 100 ppm	**Cumene** **OSHA** 50 ppm **ACGIH** 50 ppm	**Gasoline** **ACGIH** 300 ppm
			Hexane **OSHA** 500 ppm **ACGIH** 50 ppm		**Xylenes** **OSHA** 100 ppm **ACGIH** 100 ppm	**Trimethyl Benzene** **ACGIH** 25 ppm (all isomers)	

9. Data Matrix

Endpoint	Measured Data on Naphtha (petroleum), heavy coker	Data from the Gasoline Blending Streams Category	Data from the Kerosene/Jet Fuel Category	Read-Across to Naphtha (petroleum), heavy coker
Pour Point (°C)		-55	-50 to -47	< -47
Boiling Range (°C)	6 – 314			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)		2.09 to 46	18 to 25	2.09 to 46
Acute Daphnia EL50 (mg/L WAF loading rate)		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
LC_{50}		>5 mg/m^3		>5 mg/m^3
Repeat Dose (inhalation)		NOAEC = 10,153mg/m^3 (light-ends)		NOAEC = 10,153mg/m^3 (light-ends)
Repeat Dose (dermal)			330 mg/kg/d	330 mg/kg/d
In vitro Mutagenicity		Negative	Negative	Negative
In vivo Mutagencity		Negative	Negative	Negative
Developmental Toxicity (inhalation)		NOAEC > 20,638mg/m^3 (light-ends)		NOAEC > 20,638 mg/m^3 (light-ends)
Developmental Toxicity (dermal)			495 mg/kg/d	495 mg/kg/d
Reproductive Toxicity (inhalation)		NOAEC > 20,004 mg/m^3 (light-ends)		NOAEC > 20,004 mg/m^3 (light-ends)
Reproductive Toxicity (dermal)			>495 mg/kg/d	>495 mg/kg/d

10. References

Atkinson, R. 1990. Gas-phase tropospheric chemistry of organic compounds: a review. Atmos. Environ. 24A:1‑41.

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

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

API (American Petroleum Institute). 1987b. Comprehensive analytical analysis of API generic petroleum streams. Washington, D.C.

ASTM (American Society for Testing and Materials). 1999. Standard Test Method for Pour Point of Petroleum Oils. ASTM D 97, Volume 05.01. West Conshohocken, PA.

Atlas, R.M. Microbial Degradation of Petroleum Hydrocarbons: an Environmental Perspective. Microbiological Reviews. 45: 180-209; 1981.

Battelle. (1997). 13-Week subchronic dermal study with neurotoxicology evaluations of hydrodesulfurized kerosene in Sprague-Dawley rats: Final report. Battelle study No. N001450A. Battelle, Columbus, Ohio.

CONCAWE. 2001. Environmental classification of petroleum substances - Summary data and rationale. Report No. 01/54. CONCAWE, Brussels.

CONCAWE. 1996a. Physical-chemical characterization of gasoline samples: Study No. 104490. Study conducted by Exxon Biomedical Sciences, Inc. CONCAWE, Brussels, Belgium.

EIA (Energy Information Administration) 2010. http://www.eia.doe.gov/

EPA, 2006. Non-confidential 2006 IUR Records by Chemical, including Manufacturing, Processing and Use Information http://cfpub.epa.gov/iursearch/2006_iur_companyinfo.cfm?chemid=4798&outchem=comp

Harris, J.C. 1982a. Rate of Aqueous Photolysis. Chapter 8 in: W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt, eds. Handbook of Chemical Property Estimation Methods. McGraw-Hill Book Co., NY.

Harris, J.C. 1982b. Rate of Hydrolysis. Chapter 7 in: W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt, eds. Handbook of Chemical Property Estimation Methods. McGraw-Hill Book Co., NY.

Jokuty, P., Whiticar S., Wang Z., Fingas M., Fieldhouse B., Lambert P., and Mullin J.. 2002. Properties of Crude Oils and Oil Products. Environmental Protection Service, Environment Canada, Ottawa, Ontario. Internet Version 2002 via http://www.etcentre.org/spills.

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

McKee, R., Amoruso, M., Freeman ,J. and Przygoda, R. (1994). Evaluation of the genetic toxicity of middle distillate fuels. Environmental and Molecular Mutagenesis 23:234-238.

McKee, R., Schreiner, C., Nicolich, M. and Gray, T. 2010. Assessment of the *In Vivo* Cytogenetic Potential of Petroleum Derived Materials. Society of Toxicology 49th Annual Meeting, March 7-11, 2010; Abstract #340.

Mobil Corporation, 1999. 'Determination of the Aerobic Ready Biodegradability of MSDW Kerosene Mid Blend Using the OECD 301F Manometric Respirometry Test Method.' Mobil Business Resources Corp., Ecotoxicology Laboratory, Paulsboro, NJ, 1999.

Nessel, C.S. 1999. A comprehensive evaluation of the carcinogenic potential of middle distillate fuels. Drug Chem. Toxicol. 22:165-180.

OSHA, 1999. Occupational Safety and Health Administration Technical Manual, TED 1-0. 15A, Section IV. Chapter 2. http://www.osha-slc.gov/dts/osta/otm/otm_toc.html

Petroleum HPV (2008). Category Assessment Documents for Gasoline Blending Streams http://www.petroleumhpv.org/pages/gasoline.html

Petroleum HPV (2010). Category Assessment Documents for Kerosene/Jet Fuel http://www.petroleumhpv.org/pages/gasoline.html

Roy, T.A., Blackburn, G.R., Johnson, S.W. and Mackerer, C.R. 1988. Correlation of mutagenic and dermal carcinogenic activities of mineral oils with polycyclic aromatic compound content. Fund. Appl. Toxicol. 10: 446.

Roy, T.A., Johnson, S. W., Blackburn, G.R., Deitch, R. A., Schreiner, C. A. and Mackerer, C.R. 1985. Estimation of mutagenic activity and dermal carcinogenic activity of petroleum fractions based on polynuclear aromatic hydrocarbon content. Presented at the 10th International Symposium on Polynuclear Hydrocarbons, Columbus, OH. Published in “Polynuclear Aromatic Hydrocarbons: a Decade of Progress. pp. 809-824. Battelle Press, Columbus.

Schreiner, C., Bui, Q., Breglia, R., Burnett, D., Koschier, F., Podhasky, P., Lapadula, L., White, R., Feuston, M., Krueger, A. and Rodriguez, S. 1997. Toxicity evaluation of petroleum blending streams: reproductive and developmental effects of hydrodesulfurized kerosene. J. Tox. and Env. Health Vol 52, pp 211-229.

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

Shiu, W.Y., M. Bobra, A.M. Bobra, A. Maijanen, L. Suntio, and D. Mackay. 1990. The water solubility of crude oils and petroleum products. Oil & Chemical Pollution. 7:57-84.

Springborn Laboratories, Inc. 1999a. Light Alkylate Naphtha-Determination of Inherent Biodegradability. Study No. 13687.6111, Wareham, MA.

Springborn Laboratories, Inc. 1999b. Light Catalytically Cracked Naphtha-Determination of Inherent Biodegradability. Study No. 13687.6109, Wareham, MA.

Springborn Laboratories, Inc. 1999c. Light Catalytically Reformed Naphtha-Determination of Inherent Biodegradability. Study No. 13687.6110, Wareham, MA.

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

US EPA (United States Environmental Protection Agency). 2000. Estimation Programs Interface (EPI) Suite™. Washington, DC.

Vijayalaxmim,V, Kligerman, A.D., Prihoda, T.J., Ullrich, S.E. (2006) Micronucleus

Studies in the Peripheral Blood and Bone Marrow of Mice Treated with Jet Fuels, JP-8 and Jet A. Mutation Research / Genetic Toxicology and Environmental Mutagenesis . Elsevier Science Ltd, New York, NY, 608(1):82-87.

Yaws, C.L., X. Pan, and W. Lin. 1993. Water solubility data for 151 hydrocarbons. Chem. Engin. 100(2), 108-111.

11. 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

12. 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.